

UNDERSTANDING RADIOACTIVE IODINE (I^{131}) THERAPY



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HYPERTHYROIDISM is considered the most common endocrine disease of the older cat. It has been estimated that approximately 10% of cats over 10 years of age are or will be affected. The disease begins as an adenoma of one or both of the thyroid lobes. Over several years the adenoma may transform to adenocarcinoma. Treatment of the latter is much more intense and often not successful; therefore, it is highly desirable to rid the cat of the adenoma.

There are four treatments in two categories. Treatments in the “Control” category are the administration of methimazole or y/d, an iodine restricted diet. Treatments in the “Cure” category are thyroidectomy and radioactive iodine (radioiodine or I131) therapy. The obvious advantage for using a Cure approach is the avoidance of thyroid adenocarcinoma.

Each treatment approach has pros and cons. The approach with the most pros and the least cons is I131 therapy. Although its availability is somewhat limited, it can rid the cat of the benign tumor without destruction of the normal thyroid tissue or the parathyroid gland. When dosed properly, I131 therapy will cure the disease without resulting in any further treatment of the cat for thyroid disease, either hypo- or hyper-.

Since 2004 my practice, Alamo Feline Health Center, has treated over 500 hyperthyroid cats with I131. During that time many questions have arisen regarding this treatment modality. Below are the questions we have received and the answers. Note that radiation laws vary from state to state so some of the legal aspects of these answers may not apply to all states.

1. What is the cost? The treatment cost is usually based on the dose of I131 that is administered. Cats diagnosed early get a smaller dose so their treatment cost averages \$1000-1500, which includes isotope administration and the required hospitalization until discharge. Cats with advanced disease require a higher dose; however, it is very unusual for the higher doses to cost more than \$2000. In addition to the actual treatment cost, there is usually an examination/referral exam fee of \$75.00-150.00 and the cost of any needed pretreatment tests. The latter may be several hundred dollars depending on the facility and the tests performed. Some cats require sedation for safe I131 administration. There will be a charge for sedation; the cost will depend on the drug and the route of administration.

2. How is the dose determined? There is not a precise way to determine the dose of I131 for any given cat. Formerly, in the U.K., every cat received the same dose. However, notable treatment failures forced U.K. veterinarians to re-examine their dosing protocol. Despite the absence of a precise method, satisfactory dosing techniques do exist. Rather than basing dosage on the size of a cat, it is based on the size of the tumor.

The size of the tumor can be estimated in several ways. Thyroid palpation can be used in most cats. After many years of practice, we have developed a sizing system that works well. More precise size determination may be made with a technetium scan, not available at all treatment facilities.

For best results, we use a combination of palpation and total T4 (TT4) levels to determine tumor size and are correct over 99% of the time. In order to attain this level of accuracy, we need an exact TT4 value.

3. What pre-treatment laboratory tests are needed? In addition to a total T4 (or fT4), we need to be sure the kidney function is normal or nearly normal. High thyroxine levels increase heart rate and blood pressure with resulting increased perfusion of the kidneys. This process results in temporarily lowered creatinine (especially) and BUN values. Note that the higher the TT4 or fT4 the more the kidney values are lowered. Therefore, we need to have the renal values at the time of diagnosis and any values since.

4. If the cat's renal values increase above normal after treatment, what are the consequences? If the one month post-treatment values are in late IRIS Stage 2 or early IRIS Stage 3 (creatinine = 2.9-4.0 mg/dl) range, there are great options to control renal disease and slow the progression of age-induced renal deterioration. However, these cats need support quickly. If the creatinine rises to 4.0 mg/dl or greater, more aggressive therapy is needed, but this is still feasible. Note that after treating over 500 cats, we have only had 4 cats (0.8%) in the latter category.

5. What about the Methimazole Test? The "Methimazole Test" has been employed to determine what level of renal function is likely to be present after treatment with I131. Methimazole is given until the TT4 is normal (about 2-4 weeks), and then the TT4 is rechecked.

This is a test that comforts many people – veterinarians and owners alike. It gives us an understanding of what the kidneys are likely to do after I131 treatment. However, Dr. Mark Peterson, the guru of hyperthyroidism, is of the opinion that it is rarely needed. His perspective is that if hyperthyroidism exists, it needs to be treated or else it will be fatal. If the kidney values increase after treatment, renal disease can be addressed with diet, electrolyte correction, SC fluids, etc.

We will treat cats with I131 with or without a methimazole test. If one is performed, the cat needs to be off the drug for at least 5 days before I131 treatment.

6. Ordering the Isotope: By law, we are not permitted to store I131 on our premises. When it is delivered to us, we must pay for it, and it must be given to a cat. We cannot store it for future use or return it. Therefore, we do not order it until our patients are physically in the building.

7. How long does a cat need to be hospitalized? Our patients are generally treated on Mondays. Their release is governed by state rules which mandate we perform a scan to determine when the level of radioactivity is safe. Most cats are then cleared for release on Thursdays or Fridays; however, if the results of the scan are not appropriate, they stay until they are. It is very unusual for discharge clearance to go past Saturday, but I131 excretion is largely dose related. The higher the dose, the longer the isolation period must be. *NOTE: The answer to this question varies from state to state.*

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The safe level is not all the way down to zero. If the owner is concerned about the minuscule amount of residual radioactivity, we are happy to board the cat until it reaches zero. The additional stay is charged as a boarding fee only; there is no charge for further scanning.

The radioactivity is principally eliminated through the urine and the stool. If the cat does not eat while it is here, the elimination is slower and the stay prolonged. Therefore, we request that owners bring a few days of the cat's favorite food in order to encourage the cat to eat, and thus expedite the elimination process.

8. Can my clients bring bedding or toys for their cats to have during the treatment time? Yes. However, State regulations prohibit them from being returned. *NOTE: The answer to this question varies from state to state.*

9. My patient's liver enzymes are elevated. Should I perform more diagnostics or treat for liver disease? Elevation of liver enzymes (LEs), especially ALT, is expected in cats with hyperthyroidism. It is the result of prolonged TT4 elevation. The LEs will return to normal 4-6 weeks after treatment. That said, it is possible for a cat to have two concurrent diseases which elevate LEs. If you are concerned about a dual diagnosis, a liver biopsy is indicated. We can do that if you are not comfortable doing so. We generally perform a fine needle biopsy with a 22 gauge needle guided by ultrasound. However, we cannot do a liver biopsy the same day as I131 treatment due to the turnaround time required by the veterinary pathology laboratory.

10. Are there side effects? No. When the proper adenoma dose is given the effects of I131 are limited to hyperactive thyroid cells; other body cells, including normal thyroid cells, are not affected in any way. If the adenocarcinoma dose is given (5-10X adenoma) normal thyroid cells are killed, the cat becomes hypothyroid; however, no other body cells are adversely affected.

11. Can clients visit their cats? No. The State regulations prohibit this.

12. Is it permissible to administer medications for other diseases? State law prohibits us from handling these cats for the first 24 hours after treatment. If doing without medications for that period of time is life-threatening, we should not treat the cat. Although limited contact is permitted after the first 24 hours, we can then administer oral or injectable medications. *NOTE: The answer to this question varies from state to state.*

13. What post-treatment care is needed at home? There are state-mandated rules the owner is expected to follow when the cat returns home. These release criteria are listed for your clients. *NOTE: The answer to this question varies from state to state.*

14. Will this cat be a danger to my other pets at home? No. The I131 treated cat does not need to be separated from other cats or use a different litter box. Dogs that eat cat stools are also not at-risk.

15. I am not sure of the diagnosis. Should I confirm it with a free T4? The fT4 is said to be more sensitive than the TT4 for hyperthyroidism. However, in some situations it is not specific. A study published



in JAVMA (June 15, 1996) showed that cats with non-thyroidal illnesses frequently have a decreased TT4 and an increased FT4. Therefore, this test must be used with care.

Our preferred test for clarifying confusing cases is the T3 Suppression Test. It is described in *The Feline Patient*, eds. 3 and 4 or other standard textbooks.

16. What follow-up is needed after treatment? One month after treatment, the cat needs to have its TT4 and renal values determined. These tests are usually performed by the referring veterinarian, which is our preference. If any values are abnormal, the treating veterinarian should be contacted for recommendations.

17. How often does hypothyroidism occur after I131 treatment? It is not unusual for the TT4 to be subnormal at one month post-treatment. When a thyroid tumor is active, negative feedback stops TSH production causing normal thyroid cells to become dormant. When the thyroid tumor is destroyed by I131 treatment, it may take more than one month for the dormant thyroid cells to rebound. This is called “transient hypothyroidism.” If the TT4 is subnormal at one month post-treatment, repeat it four to six weeks later. “Persistent hypothyroidism” following treatment is dose related and occurs less than 1% of the time in the cats we treat.

18. I understand that a thyroid (technetium) scan can differentiate a thyroid adenoma from a thyroid adenocarcinoma. Is that correct? No. Thyroid disease begins as a thyroid adenoma. Over time, the benign adenoma may transform to a malignant thyroid adenocarcinoma. It is frequently stated that 2% of hyperthyroid cats have malignancy, but it should be noted that these are the cats with advanced disease. Therefore, a cat with early or mid-range thyroid disease is extremely unlikely to have adenocarcinoma.

A thyroid scan can determine the number of thyroid masses and their sizes and give a suggestion of differentiation. However, a histological diagnosis can only be made by a pathologist with a microscope. If malignancy is suspected, a thyroid biopsy is the only way to accurately differentiate thyroid adenoma from thyroid adenocarcinoma.

19. Does treatment with methimazole or y/d prevent the transformation from adenoma to adenocarcinoma? No. Neither of these treatment modalities destroys the thyroid tumor. Over time, the tumor gets larger requiring higher doses of methimazole to control the disease. We do not know the long-term success rate and long-term side effects of y/d.

Dr. Mark Peterson reported on a large number of cats on methimazole for four years. He found the incidence of malignancy to be about 20%. Only destroying the benign tumor can prevent its change to adenocarcinoma.

20. Can thyroid adenocarcinoma be treated successfully? Possibly. The size of the tumor and the extent of metastasis are the major determinants in success and survival. In order to have a realistic chance of remission, the dose of I131 is increased about 5-10 fold. Some survive 1-2 years and have quality life for most of that time. However, this very high dose of I131 will kill normal thyroid tissue leaving the cat persistently hypothyroid. These cats need thyroid replacement hormone therapy for the remainder of their lives.

The poor response rate for thyroid adenocarcinoma means that cure (not just control) during the stage of adenoma is highly desirable. Radioactive iodine has the ability to do this.