



# **Hot Topics in Feline Medicine Online 'Mini Series'**

**Session 3:  
Thin Cats, Fat Cats!**  
Feline Hyperthyroidism and Diabetes Mellitus

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## Hot Topics in Feline Medicine Part 3

### Feline hyperthyroidism: what's new?

Hyperthyroidism is well recognised to be the most common feline endocrinopathy encountered in clinical practice. Whilst the majority of cases are straightforward to diagnose and treat, there are also many cases that prove to be much more challenging. It is important that the clinician recognises the potential difficulties in diagnosis and management, and the complications that may arise, to enable owners to be well-informed and involved in the decision making as to the most appropriate treatment option for their cat.

The majority of thyroid tumours are benign, characterised histologically as adenomatous hyperplasia or adenomas. In approximately 75% of cats, both thyroid glands are involved. Since there is no physical connection between them, this has led to speculation that development of hyperthyroidism may be influenced by some sort of circulating factor. There have subsequently been some associations made with development of hyperthyroidism and feeding of tinned food (particularly fish or liver and giblet flavoured food), being kept indoors, and use of cat litter, exposure to flea sprays, fertilizers, insecticides and herbicides. However, the precise relationship between these risk factors and development of hyperthyroidism is not known. It has also been speculated, but not proven, that certain autocrine or paracrine growth factors, circulating thyroid stimulators or genetic mutations in TSH receptors may have a role in the development of hyperthyroidism.

Malignant thyroid carcinomas however can also be a cause of hyperthyroidism, occurring in approximately 1-3% of hyperthyroid cats. Carcinomas may present in a variety of ways; they can be solitary masses involving only one lobe, they can involve both lobes and appear as simple bilateral disease, there may be multiple nodules in the cervical region, or there may also be ectopic tissue beyond the thoracic inlet. They can be functional carcinomas (i.e. cause hyperthyroidism) or may be non-functional (i.e. do not cause hyperthyroidism). **Since adenomas and carcinomas cannot be distinguished clinically or on gross appearance, it is important that thyroid tissue is submitted for histopathology following all thyroidectomies.**

### Clinical signs

The clinical signs associated with hyperthyroidism are well known (summarised in Figure 1) and not many veterinary surgeons would miss a 'classic' hyperthyroid cat with weight loss, polyphagia, and tachycardia. However, not all hyperthyroid cats will have these classic signs and most veterinarians are managing to detect hyperthyroidism at much earlier stages now.

For example, often vomiting or restlessness may be the only initial clinical sign, or in some cases goitre may be detected as an incidental finding on a clinical examination before an owner has even noticed any change in the cat.

As illustrated in Figure 1, a huge variety of signs can be attributable to hyperthyroidism, and sometimes the less common clinical signs can be present without any of the more common ones, for example tremors, panting (open-mouth breathing with no underlying thoracic pathology) or profound muscle weakness. Some cats also exhibit what is known as ‘apathetic hyperthyroidism’, where rather than being polyphagic and hyperactive, they are inappetent and lethargic. Concurrent illness, which is common in this age group of cats, may also complicate the clinical picture

**Figure 1 – Historically reported clinical signs of hyperthyroid cats**

(taken from Felman & Nelson, Canine and Feline Endocrinology & Reproduction, 3<sup>rd</sup> Ed)

Clinical sign	% of cats
Weight loss	92
Polyphagia	61
Polydipsia/polyuria	47
Increased activity/restlessness	40
Diarrhoea/ increased frequency/ bulky stool/ steatorrhea	39
Vomiting	38
Skin changes (patchy alopecia, matting, dry coat, seborrhoea, thin skin)	36
Dyspnoea/panting/coughing/sneezing	23
Inappetance	14
Lethargy	11
Weakness	10
Tremors/seizures	7
Heat intolerance	5
Haematuria	2
Neck ventroflexion	<1

## Diagnosis

Palpable goitre is reported to be present in around 90% of hyperthyroid cats, although in a recent survey of 80 hyperthyroid cats seen at UOB Feline Centre, only 72% had a palpable goitre. This figure is likely to be significantly skewed as this is a referral population, but nevertheless demonstrates that lack of a palpable goitre certainly does not exclude hyperthyroidism. Equally, palpation of a cervical mass is not pathognomonic for hyperthyroidism, since non-active thyroid nodules can occur, in addition to cervical masses of other origins.

Definitive diagnosis of hyperthyroidism is usually based on demonstration of an elevated serum total T4 concentration. Although there are in-house T4 analysers now available, they do not appear to be very reliable, and therefore samples for T4 measurement should always be sent to a reliable external laboratory. **Elevated total T4 is very specific for hyperthyroidism, and in more than 90% of hyperthyroid cats this alone will be enough to confirm the presence of hyperthyroidism.** However in a small percentage of hyperthyroid cats, total T4 can be within the normal range, although usually at the top of the normal range. This may be due to normal T4 fluctuations in an early/mild hyperthyroid cat, or due to suppression of T4 as a result of concurrent non-thyroidal illness. If total T4 is normal in a cat that is strongly suspected as being hyperthyroid, the total T4 should first be repeated, and if still normal a free T4 performed by equilibrium dialysis. Free T4 is less specific than total T4 (i.e. cats without hyperthyroidism, may have elevated results, it is affected by other diseases), but is also more sensitive so will usually be elevated in early, mildly hyperthyroid cats.

### Figure 2 – Further diagnostic tests for hyperthyroidism

If total T4 is within normal range in a suspected hyperthyroid cat:

1. Repeat total T4 & exclude non-thyroidal illness
2. If still in normal range perform free T4 by equilibrium dialysis
3. If both still normal, consider either of the following:
  - a) Wait, monitor the cat & repeat steps 1&2 two-three months later
  - b) T3 suppression test
  - c) TRH stimulation test
  - d) Thyroid scintigraphy

**Figure 3 - Protocol for T3 suppression test**

<ol style="list-style-type: none"><li>1. Obtain serum for measurement of T3 and T4 concentrations</li><li>2. The following morning begin administration of 25µg T3 orally three times daily (i.e. every 8 hours) for two days</li><li>3. Administer a 7<sup>th</sup> dose in the morning of day 3</li><li>4. Take second blood sample for serum T3 and T4 2-4 hours after administration of last dose</li><li>5. Submit pre- and post-treatment samples to lab at same time to avoid any possible interassay variation</li></ol>
<p>Interpretation:</p> <ul style="list-style-type: none"><li>• Normal cats should demonstrate marked reduction in serum T4</li><li>• Hyperthyroid cats show minimum or no decrease in serum T4</li><li>• T3 results confirm whether T3 was successfully administered so should increase in normal and hyperthyroid cats</li></ul>

**Figure 4 - Protocol for thyrotropin-releasing hormone (TRH) stimulation test**

<p>Collect blood for total T4 measurement before and 4 hours after intravenous administration of 0.1mg/kg TRH</p> <p><b><i>NB adverse reactions are common including salivation, vomiting, tachypnoea, defaecation</i></b></p>
<p>Interpretation:</p> <ul style="list-style-type: none"><li>• Normal cats and cats with non-thyroidal illness usually have a two-fold increase (&gt; 60% increase is diagnostic) in serum T4</li><li>• Hyperthyroid cats have little or no increase (&lt;50% increase) in serum T4</li><li>• 50-60% increase in serum T4 is non-diagnostic</li></ul>

### ***Measurement of feline TSH***

In theory measuring TSH might help in the diagnosis of hypoT4 in cats with mild/early hyperthyroidism and a high normal T4. Studies have shown that hyperthyroid cats have a low or undetectable TSH level. However, the issue with this test remains that some normal cats will have low levels of TSH. This maybe due to the fact that the only available test is the canine TSH assay and it only detects 35% feline circulating TSH. So until a feline TSH assay is available results should be interpreted with caution and the test used only to EXCLUDE hyperthyroidism if the TSH is normal.

### ***Thyroid scintigraphy***

Thyroid scintigraphy is an extremely useful technique that can assist in the diagnosis of hyperthyroidism in borderline cases, but also is invaluable in assisting in the decision making regarding the most appropriate treatment option.

Radioactive technetium-99m (pertechnetate) is administered by intravenous injection and the cat is then scanned with a gamma camera approximately 20 minutes later. The technetium-99m is trapped and concentrated within thyroid follicular cells because the pertechnetate ion mimics that of iodide, but unlike radioactive iodine it is not incorporated into the organic thyroid hormone and therefore is not retained in the thyroid gland, but is excreted via the kidneys. Pertechnetate emits low energy  $\gamma$ -particles and has no  $\beta$ -emission, and so is safe to use. It also has a short half life of 6 hours, meaning that cats do not have to remain in isolation with limited handling for long periods. Following administration, the cat has to remain in the radioactive isolation unit for 2 days before it can be discharged.

Scanning the thyroid following technetium-99m administration produces an image of all functioning thyroid tissue. In addition to the thyroid tissue it also concentrates in the salivary glands and gastric mucosa. Hyperthyroidism can be diagnosed when the uptake in the thyroid glands is greater than that in the salivary glands. The location of the hyperfunctional thyroid tissue and the number of hyperfunctional areas can be identified. The scan can therefore be used to determine whether surgical treatment is possible, and if so whether a unilateral or bilateral thyroidectomy is required and the precise location of the tissue to be excised. It will also illustrate if there is ectopic tissue present, in which case surgical treatment would not be effective.

In the literature the percentage of hyperthyroid cats with ectopic tissue is generally quoted as being around 3%. However, a recent survey of 120 hyperthyroid cats seen at the University of Bristol between 1994 and 2004 revealed that 15% of them had ectopic thyroid tissue within the thorax, and a further 53% had thyroid nodules within the thoracic inlet, which may have been less surgically accessible. Although again, these figures will be skewed being a referral

population, when we looked at the reason for referral not many of them were referred because of recurrence of hyperthyroidism following surgery, often they had been referred because of owners wishing to explore the possibility of radioactive iodine treatment. 28 out of the 120 cats had undergone previous thyroidectomies, and of these cats, 17 cats (61%) had ectopic intrathoracic hyperfunctioning thyroid tissue. Out of the 26 cats that had hyperfunctioning thyroid tissue in the thorax, 10 of these cats also had a palpable goitre, again illustrating that the presence of a palpable goitre does not mean that removing it will cure the hyperthyroidism. In addition some cats had up to 5 separate hyperfunctioning areas. **Always warn owners before performing a thyroidectomy that a percentage of cats will have hyper-functional thyroid tissue elsewhere in the body meaning surgery is NOT curative.**

Although there have been some descriptions in the literature of scintigraphic findings in cats with thyroid carcinomas, in our experience, thyroid carcinomas have very varied scintigraphic appearances and cannot be distinguished from adenomatous hyperplasia on the basis of scintigraphy. In the 12 cats with thyroid carcinomas seen at the University of Bristol, the scintigraphic findings have included single small nodules in the neck or thoracic inlet, single very large nodule in neck, multiple nodules and nodules in the thorax, and all of these appearances have also been seen in cats with adenomatous hyperplasia.

Although thyroid scintigraphy is available in a few first opinion clinics, it is largely a referral procedure. Clearly it is unrealistic to refer every hyperthyroid cat before considering a thyroidectomy, and many cats undergo curative thyroidectomies with no complications. However, given the number of cats that we are seeing with ectopic thyroid tissue, the author advises that at least the potential for presence of ectopic tissue and recurrence of hyperthyroidism and the option of referral for further evaluation and thyroid scintigraphy should be discussed with every owner prior to performing surgery.

## **Treatment**

The 3 treatment options for hyperthyroidism are widely known, however the majority of hyperthyroid cats seen in first opinion practice are treated either with surgical thyroidectomy or medical management with methimazole (felimazole®; Arnolds), or carbimazole (Vidalta®; Intervet-Schering Plough).

The obvious disadvantages of long term methimazole or carbimazole include the requirement for life-long treatment and regular monitoring, and potential side effects such as anorexia, vomiting, hepatopathies, facial pruritus and haematological disorders. Although coagulopathies have not been definitively linked with methimazole treatment, the author is aware of a number of cats with unexplained coagulopathies that have resolved following withdrawal of methimazole treatment, and therefore would recommend that where possible

coagulation times are assessed prior to surgery in cats receiving this treatment. As a result of the severity of some of the potential side effects, it is currently advised to begin treatment with a low dose and then to increase to effect if no adverse signs are seen. Transdermal methimazole treatment has also been investigated, and has been used widely in the US with good results in a proportion of cats.

Carbimazole is an alternative anti-thyroid drug, which is metabolised to methimazole following absorption. This is licensed (Vidalta®; Intervet-Schering Plough) as a slow release formulation designed for once daily dosing. There are no comparative studies between methimazole and carbimazole with regard to prevalence of adverse effects, and in theory as carbimazole is metabolised to methimazole it seems unlikely that there would be less adverse effects observed with carbimazole. However, anecdotally many veterinarians have the impression that more frequent and more severe adverse effects are observed with methimazole compared to the previously used carbimazole in the unlicensed form of Neomercazole®. However there is no evidence to support this, and it is too early in the use of Vidalta® to know the prevalence of adverse effects observed with this drug. The most useful benefit of Vidalta® is the need to only administer once daily, which is likely to improve client compliance and thereby improve treatment success.

**Medical management** however is particularly useful for the treatment of cats with concurrent disorders that may increase the risk of anaesthesia or the isolation time required with radioactive iodine treatment. It is also invaluable in stabilising hyperthyroid cats prior to surgery, and to allow re-assessment of renal function once the cat has become euthyroid, before undergoing a more irreversible treatment. It is advisable that all cats, but especially those with any evidence of renal dysfunction (elevated urea/creatinine, suboptimal urine SG) receive a trial treatment of methimazole with follow-up serum biochemistry and urinalysis, prior to pursuing 'permanent' therapy.

**Surgical thyroidectomy** remains a good choice of treatment in cats where this is no ectopic hyperfunctional thyroid tissue. Cats should be appropriately stabilised with medical therapy, prior to surgery, to reduce anaesthetic risk. The main complication associated with thyroidectomy is the development of post-operative hypoparathyroidism and subsequent hypocalcaemia. In most instances, this will resolve with time, and treatment with calcium supplementation and vitamin D is only required in the short term until parathyroid function is regained. However, occasionally cats can remain hypoparathyroid and require long term treatment with vitamin D +/- calcium supplementation.

**Radioactive iodine treatment** is an excellent treatment option, and would be the treatment of choice in most hyperthyroid cats if it was not for the big disadvantages of limited availability, and post-treatment isolated hospitalisation time. Radioactive iodine is also the treatment of choice for functional thyroid carcinomas, although the dose required for these cats is approximately 10 times higher than that required to treat adenomatous



hyperplasia/adenomas, because carcinomas are less efficient at concentrating and retaining iodine. To the authors knowledge, there are currently 4 referral centres in the UK that offer radioactive iodine treatment; the University of Bristol, University of Edinburgh, RVC and The Animal Health Trust, and 2 first opinion practices; Barton Veterinary Hospital in Canterbury and The Cardiff Cat Clinic. The University of Bristol is the only one of these centres licensed to use the much higher doses required for treatment of thyroid carcinomas.

Iodine-131 is the isotope used for treatment. The iodine is concentrated within the thyroid gland and its emitted radiation destroys surrounding functioning thyroid cells. It is  $\beta$ -particles that causes most of this damage, and because they travel <2mm in tissue, radiation damage does not affect surrounding structures. Thyroid cells that are not destroyed immediately develop abnormalities reducing their survival time. The thyroid damage therefore is both immediate and ongoing, resulting in euthyroidism usually within 4-30 days, although a small proportion of cats can take significantly longer to become euthyroid.

The treatment is given via a single subcutaneous injection. No anaesthesia is required, although many some centres will sedate the cats (usually a ketamine/midazolam combination) to avoid the health and safety implications if the cat wriggled and radioactive iodine was spilt. Over 95% of cats will become euthyroid after a single treatment, but in a small number of cats, the first treatment is insufficient. Once euthyroid, the treatment is permanent.

It used to be advised that cats needed to be off oral anti-thyroid drugs for at least 2 weeks before radioactive iodine administration. The concern was that because the drugs inhibit the organification of iodide and coupling of iodotyrosyl groups this may interfere with the efficacy of the radioactive iodine therapy. The general consensus now appears to be that methimazole does not interfere with radioactive iodine treatment, however this is controversial.

Due to radiation safety regulations, cats are required to spend a period of time in an isolation ward with minimal staff contact following treatment, until the radioactivity levels have reduced. Since iodine-131 has a long half life, of 8.1 days, this isolation period tends to be quite lengthy. The precise length of the isolation time however, varies between centres, and is decided upon by the local radiation safety officer. At Bristol Vet School it is 3 weeks for 'normal' hyperthyroid cats. For cats with thyroid carcinomas, it is 7 weeks, due to the much higher dose of iodine required. During this time the cats are hospitalised in a dedicated isolation facility. If the cat is discharged after these time periods, the owner is not required to continue any further safety precautions. However, in centres that are able to discharge cats more quickly following treatment, further safety precautions should be undertaken for a further 2-3 weeks, such as keeping the cat indoors, minimal handling and otherwise keeping >30cm distance from the cat, washing hands after handling, careful disposal of litter and no contact with children or pregnant women.

The main implication of this isolation period is that the cats can not be monitored as closely as they would be in a normal ward, and if any problems do occur whilst in there, they can receive only limited treatment and diagnostic procedures. For these reasons, radioactive iodine treatment is not the treatment of choice for every patient. Ideally, detailed investigations should be performed in hyperthyroid cats (Figure 5) to fully evaluate the cats' hyperthyroidism and any subsequent complications, as well as looking for any concurrent diseases that may not be causing the cat a problem at this stage, but could lead to complications during the isolation time. In particular scintigraphy is an important part of this evaluation as it allows the location of hyperfunctional thyroid tissue to be visualised. If for example, the cat only had cervical thyroid tissue and did not have other complications that contraindicated anaesthesia, such as severe secondary cardiac changes then surgical thyroidectomy may be a better treatment choice for some of these cats. If, however scintigraphy demonstrated the presence of ectopic thyroid tissue, then surgical thyroidectomy would not be a curative treatment and iodine or continued medical management would be the only options.

**Figure 5: Investigations performed in hyperthyroid cats prior to radioactive iodine treatment**

Investigation	Reason
Routine haematology	To assess for evidence of any other concurrent diseases, particularly renal disease, diabetes mellitus and neoplastic diseases
Serum biochemistry	
Urinalysis	To further evaluate renal function
Systolic blood pressure	Hypertension relatively common in hyperthyroid cats and may require specific treatment
Echocardiography (+/- ECG)	To evaluate cardiac parameters, given that ventricular hypertrophy is common in association with hyperthyroidism
Thoracic radiography	To assess for evidence of congestive heart failure, or any concurrent thoracic pathology
Abdominal ultrasound	To further assess for evidence of any other concurrent diseases such as neoplasia
FeLV/FIV serology	May alter prognosis
Thyroid scintigraphy	To assess if unilateral or bilateral disease and if any ectopic tissue is present

**Figure 6: Indications for radioactive iodine treatment**

- Lack of palpable goitre
- Presence of ectopic intrathoracic thyroid tissue identified on scintigraphy
- Presence of large thoracic inlet thyroid nodule(s)  
(either of these can be demonstrated by scintigraphy, or may be suspected if a cat has remained hyperthyroid following a thyroidectomy, or become hyperthyroid again some time after having thyroidectomy)
- Presence of functional thyroid carcinoma
- Contraindication for anaesthesia e.g. heart disease
- Owner treatment preference and no contraindications for radioactive iodine

**Figure 7: Contraindications for radioactive iodine treatment**

- Presence of concurrent disease e.g. abdominal or thoracic neoplasia, diabetes
- Presence of severe complications e.g. congestive heart failure
- Very uncontrolled chronic hyperthyroidism where hyperthyroid complications (e.g. heart disease, weakness, malnutrition) would be a risk
- Presence of renal insufficiency that has not been first evaluated after stabilisation with carbimazole/methimazole treatment
- Inappetent patient
- Patient that does not adapt well to hospitalisation
- Owner reluctance

### Algorithm for recommended management of hyperthyroidism

Hyperthyroidism confirmed & routine haematology/biochemistry/urinalysis performed to evaluate for concurrent disease, particularly renal disease



Systolic blood pressure measured if possible



If >200mmHg consider additional anti-hypertensive treatment (amlodipine)



If 170-200mmHg re-evaluate  
after starting methimazole/carbimazole therapy



If no complications/concurrent diseases, all 3 treatment options discussed with owner together with pros and cons of each, and need for initial stabilization with methimazole/carbimazole to evaluate renal function advised



Methimazole/carbimazole treatment initiated for stabilisation, after discussion of potential side effects



Total T4 concentrations re-evaluated after 2 weeks  
(dose increased if euthyroidism not achieved & no side effects occurred)



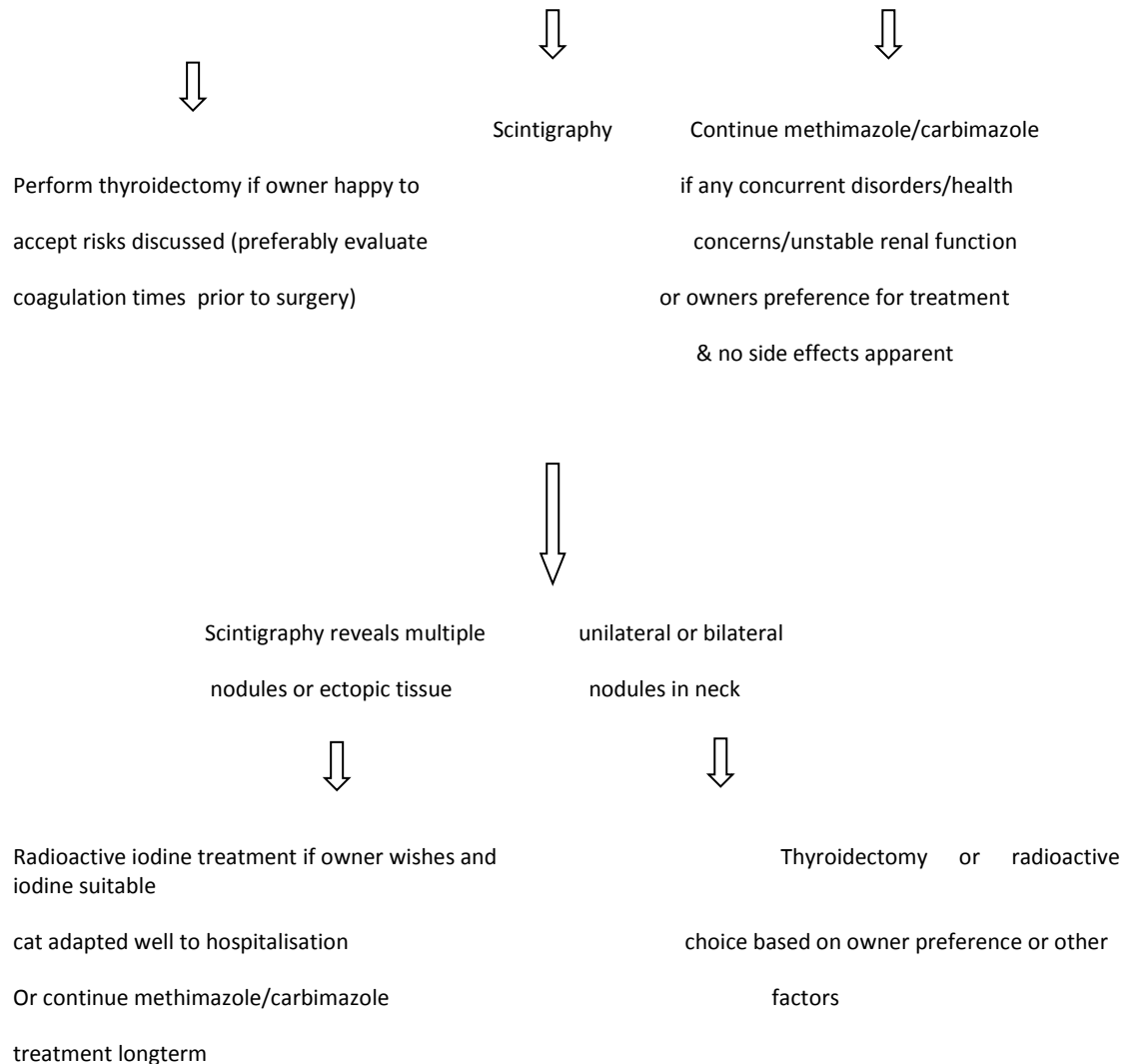
Once euthyroid, re-evaluate renal function with serum biochemistry and urinalysis



If renal function stable, further discuss with owner surgical and radioactive iodine treatment

If owner wishing to consider 'permanent' treatment option, discuss further imaging (x-ray, ultrasound, echocardiography) to further evaluate general health, exclude concurrent diseases such as neoplasia, and evaluate heart to assess anaesthetic risk. Discuss risks of surgery and potential for presence of ectopic thyroid tissue.

Offer referral for above evaluations and scintigraphy



## **Dietary treatment of hyperthyroidism**

Most people are now aware/and or using the new Hills y/d diet. The theory of the diet is that an iodine deficient diet can result in lower T4 concentrations when fed as the sole diet. The diet is also said to have reduced phosphate and sodium. There are a few points to consider:

- Prescription diets are subject to different regulations than medications and these are much less strict regards side effects/long term issues, controlled testing etc (FDA approval not needed).
- y/d has 27% protein and 23% carbohydrate which is 2.5-5 times more carbohydrate than a cat's natural diet – is this relatively high CHO level a concern in this group of patients? Certainly it should not be fed to diabetics or cats in diabetic remission
- The dry diet has little meat protein being mostly made up of vegetable protein sources (inc. soy which may be a goitrogen)
- The diet must be fed exclusively and hunting may interfere with it's effect
- The long term studies have not been done/published. Could it increase the risk of the thyroid mass growing/becoming a carcinoma? The hyperthyroidism is not being 'treated' so the disease will progress
- Palatability is an issue and nutrition is vital in this patient group
- Without long term studies we don't know the effect of a low iodine diet, in humans concerns regards immune function are raised in low iodine areas of the world – Hill's have not produced any info on immune function in cats fed y/d.

I personally feel it may have a role but does NOT replace permanent treatments such as surgery and radioiodine and that Hills need to publish more studies on long term use of the diet in terms of muscle mass (as it is high in CHO) and glucose tolerance (again due to the high CHO) as well as immune function. Also I would not be comfortable feeding it to a euthyroid cat in the same house due to the above concerns.

## Feline diabetes: challenges and frustrations!

The number of diabetic cats is on the increase. This is likely due to increased recognition as well as increased obesity in cats. In the UK nearly 1 in 200 cats are diabetic (even more prevalent in certain breeds – Burmese). Feline diabetes is often challenging to manage, leading to much confusion and owner/vet frustration. Cats are not dogs when it comes to this disease for sure and this species need to be approached differently in terms of monitoring and treatment. Major differences between dogs and cats are illustrated in the table below.

<b>DOGS</b>	<b>CATS</b>
Type 1 DM	Type 2 DM
Obvious clinical signs e.g. PU/PD	Subtle signs and PU/PD may not be noted
Usually life-long insulin requirement	Often transient insulin requirement
More predictable insulin response	Large variation in response to insulin & duration of actions
Stress hyperglycaemia not a significant concern in most dogs	Stress hyperglycaemia makes diagnosis difficult (as well as monitoring)
Predictable post-prandial hyperglycaemia	Significant post prandial hyperglycaemia doesn't occur
Defined meal times recommended	Ad lib feeding usually recommended
High fibre, high complex carbohydrate diet recommended	High protein, low carbohydrate diet recommended
Usually polyphagic if hypoglycaemia	Don't usually become polyphagic when hypoglycaemic

### Aetiology of DM in cats

Cats differ from dogs and humans as they are most commonly type 2 diabetics (although with the rise in obesity in humans type 2 is getting more common) as appose to type 1. The classic dog type 1 diabetes usually results from immunologic destruction of pancreatic beta cells but the type 2 pathophysiology is more complex.

Hyperglycaemia resulting in DM is due to a combination of the following in cats:

- Lack of insulin production
- Lack of insulin sensitivity
- Hepatic gluconeogenesis (as a response to perceived lack of insulin, ketones are a by-product)

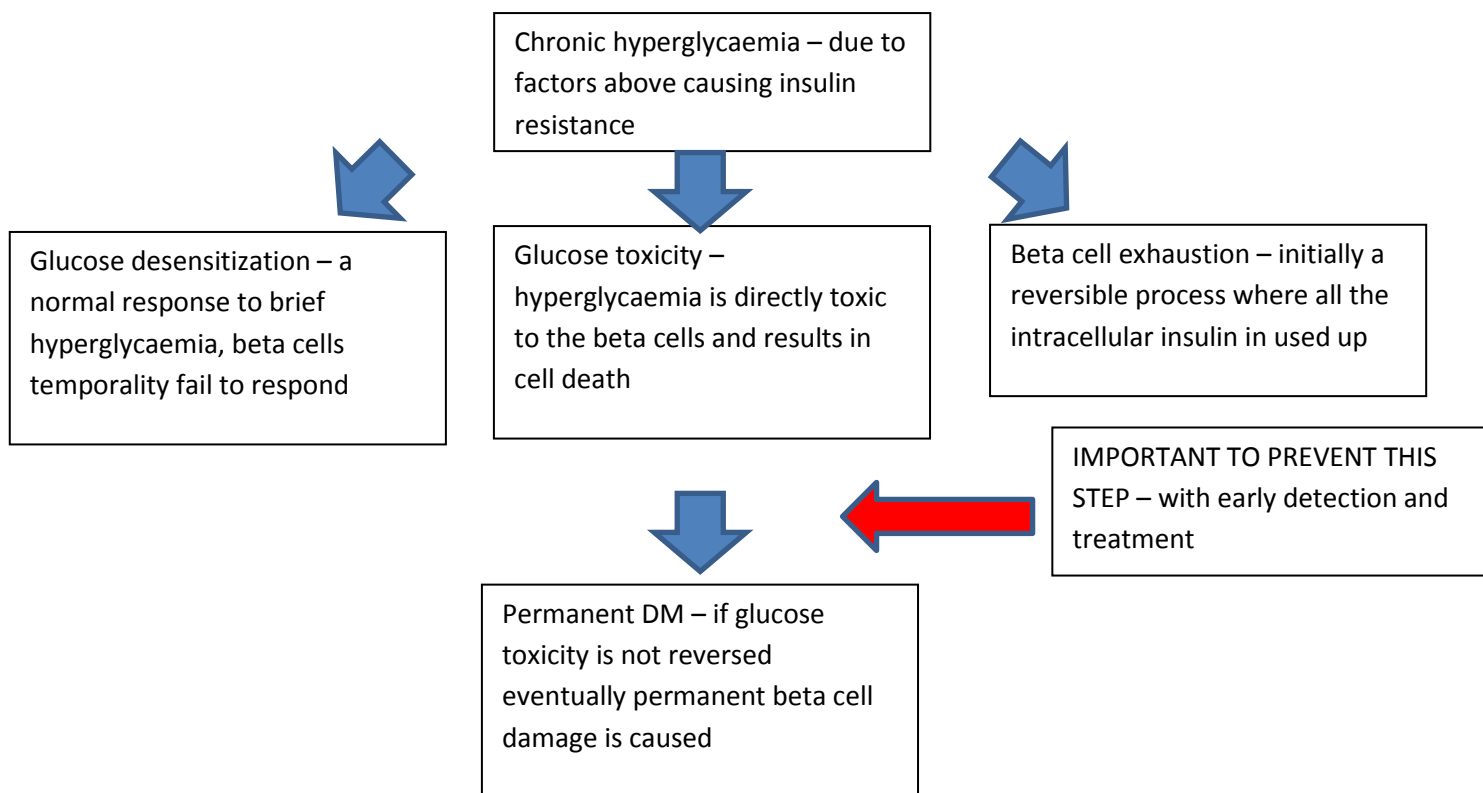
The initiating factor in type 2 DM is insulin resistance which may be associated with a decreased number of insulin receptors, reduced receptor activity or an effect on the glucose transport system that allows glucose to enter the cell. Initially the body simply produces more insulin but this is a road to nowhere as eventually beta cell failure will occur.

***Underlying causes of/risk factors for of type 2 DM***

- Pancreatitis – this certainly plays a role in the development of DM in cats (as illustrated by the number of diabetic cats with increased PLI)
- Obesity – this is directly related to insulin resistance in cats and humans. It reduces GLUT4 expression (a glucose transport protein) as well as affecting other areas of glucose handling. The beta cells eventually fail to compensate for the insulin resistance. **Appropriate weight loss is vital in management and prevention of DM!** Inactivity is also a factor here – a greater issue in indoor cats
- High carbohydrate diets – cats have very low levels of an enzyme called glucokinase which is a 'glucose sensor' – this altered glucose-sensing pathway may be an adaption to a low carbohydrate diet. So when fed a high-CHO diet, in combination with a factor causing insulin resistance – this = DM
- Additional diseases/infections – systemic inflammation can affect glucose control, cytokines may cause insulin resistance. This emphasizes the need to control infections to achieve good control of DM
- Drugs such as glucocorticoids impair glucose uptake and enhance hepatic gluconeogenesis, progestogens similarly can result in hyperglycaemia
- Genetics – Burmese cats are more likely to become diabetic in Australia, NZ and the UK. Multiple genes are involved (as in people) and this group should be monitored closely as they get into middle/older age

Hyperglycaemia itself affects the body's response to insulin. Chronic hyperglycaemia results in beta cell exhaustion but importantly this can be reversible if the factors causing hyperglycaemia can be managed. The diagram below illustrates the phenomenon of **glucose toxicity**.





In 50-60% of cats, diabetes mellitus may be transient, and with reversal of the above factors causing insulin resistance and glucose toxicity cats can revert to a non-diabetic state. This occurs most typically within 1-3 months of initiating insulin treatment. Some cats then remain subclinically diabetic never requiring further insulin treatment, whilst other cats may revert to an insulin dependent state again in the future particularly when subjected to further risk factors (e.g. becoming obese, receiving corticosteroid treatment).

### ***Diagnosis of diabetes***

Classic clinical signs are often present, but will overlap with other conditions (e.g. PU/PD and weight loss in chronic kidney disease). Take the opportunity to examine the cat thoroughly for factors that can cause insulin resistance and complicate treatment (e.g. obesity, skin/oral infections, hyperadrenocorticism, acromegaly) and alternative diseases that could explain the clinical signs or complicate the DM (e.g. hyperthyroidism, CKD).

It is important to take into account the effect of stress on glucose in cats – catecholamines stimulate hepatic glucose production and glucose handling is also affected. Therefore diagnosis cannot be made on simply the documentation of a high blood glucose (BG). Remember cats may not look externally stressed for this to occur (subtle signs are mistaken for calmness!). The hyperglycaemia can also last all day in some cases.

Stress hyperglycaemia has been reported to cause a blood glucose up to 60mmol/l!! Urine glucose will of course also be elevated. Simply assessing a urine glucose at home can be helpful here as it will often be negative.

Urine samples can easily be obtained from cats that will use a litter tray by temporarily replacing the normal litter with a non-absorbable litter.

- **Urine bacterial culture should also be performed on all newly diagnosed diabetic cats since urinary tract infections secondary to glucosuria are common, will not necessarily cause any clinical signs, and will result in insulin resistance if left untreated.**

Fructosamine must be measured as a diagnostic test for DM but remember a few limitations:

- It provides an average BG for about a week prior to testing
- It will be falsely lower in hyperthyroid cats and those with hypoalbuminaemia
- It could be normal/just above normal in a cats with early DM or mild hyperglycaemia (<17mmol/l)
- In cases where it is not convincing serial urine testing and blood testing will help clarify the diagnosis
- The vast majority of cats with DM will have fructosamine > 400µmol/l

Other testing may be indicated depending on the clinical exam, e.g.T4, imaging – **remember that identifying complicating conditions now helps prevent frustration later when the cat doesn't respond well to insulin!**

### ***Prevention of DM and early diagnosis***

Prevention is obviously desirable and so with our increased knowledge of DM in cats we need to identify the at risk cats and attempt to prevent the disease as follows, this will also allow detection of cases early – before they become permanently diabetic or emaciated and much more challenging to treat:

- Weigh cats at every consult/vaccination and refer overweight cats to a nursing clinic to discuss diet and weight loss BEFORE they become obese
- Recognise life stages that are associated with weight gain (after neutering, middle age) and prevent the weight gain before it happens (e.g. neutered cat diets, advice on exercise and activity in indoor cats) – **consider that ideally all cats over the age of 7 years have a yearly urinalysis performed!** Utilise home urine sampling, using a non-absorbent litter (e.g. Katkor/Mikki litter/aquarium gravel in litter tray)
- Pre-anaesthetic bloods should include a glucose measurement

- Ask owners of cats in at risk groups (middle aged, obese, Burmese cats) to bring a urine sample with them to consults (even just vaccinations) to identify problems early
- Advise owners of indoor cats on methods to increase activity – see FAB website and indoor cat initiative
- Client education may help prevent development of diabetes in some ‘at risk’ cats by preventing obesity and promoting exercise – see <http://www.catprofessional.com/overweight.html> for a great owner manual! (Biased I know but owner info can really help a weight loss plan).
- Owners should be warned about the risk of diabetes mellitus with use of diabetogenic drugs
- Cats receiving diabetogenic drugs should be monitored for development of diabetes
- Extra caution should be taken when using diabetogenic drugs in cats with additional risk factors
- Always follow up a high blood glucose or glucosuria with a serum fructosamine measurement
- **Always use ‘cat friendly practice’ principles to reduce stress in the practice to make blood glucose easier to interpret!**

### ***Management of DM in cats***

The treatment goals for feline diabetes mellitus have changed in recent years with the realisation of how common ‘transient’ diabetes mellitus is in cats. Whereas years ago the goal of treatment may have been to simply control clinical signs of the disease, the goals now are:

- **Early detection**
- **Aggressive treatment early in the course of the disease**
- **Aiming for diabetes to be transient with only a temporary need for exogenous**

### ***Owner factors***

We must not underestimate how much of a ‘big deal’ injecting a cat daily is. A recent study in the UK showed that having a diabetic cat did have a negative impact on people’s lives with concerns such as going on holiday, worry about the disease, worry about hypoglycaemia and so on. Therefore client management is important here and tips include:

- Manage expectations – warn owners there is no ‘quick fix’ and adjustments in dose will be needed, they need to allow 3-6months for stability also warn about ups and downs in treatment and potential complications
- Provide enough information about diabetes at initial consult – have some info packs for owners to take home

- Explain insulin requirements may be transient if prompt and aggressive treatment (which may also then be cheaper in the long term)
- Utilise nursing staff to train and listen to owners. They need time to assimilate the info and practice the injections, they will be very daunted initially by the idea of needles etc
- Be flexible with instructions regarding timing of feeding and insulin administration and realistic in what the client can achieve – for example missing insulin dosing a day a week is better than not treating at all
- Emphasise the differences between human DM and feline DM as they may feel negative about the complications of human DM
- Do not worry if an owner can not adhere to a strict dosing regime; it is better to have 5 days of twice daily dosing and 2 days of once daily dosing than for a cat to be euthanased because the owner is worried about being unable to inject twice daily

Management of DM should be considered as multimodal approach (like CKD) where insulin is important but it is not the only factor. Other issues should be addressed at the same time including diet, management of obesity, management of pancreatitis, comorbid disease, diabetogenic medications.

- Note that **Oral hypoglycaemic agents are not advised as a first line treatment, unless there is a good reason for being unable to use insulin** – this is because they have not been shown to be very effective in cats and have side effects

As early treatment to reduce glucose toxicity is a must – insulin therapy will be needed. The following are general rules!

- ***Cats can be very unpredictable in their response to insulin administration and no one type of insulin or dosing regime will be suitable for all cats***
- ***Twice daily*** dosing regimes are usually more effective (doses are quoted per injection, not per day)
- Insulin doses should not be increased by more than ***0.5 IU per injection at a time***. Following any increase in insulin dose, at least 3-5 days (preferably one week) should be left before making any further increases in dose. This is because it takes 3-5 days for glucose homeostasis to adjust after starting or altering insulin doses
- **Twice daily dosing of an intermediate acting insulin (e.g. Caninsulin) is a good first choice**
- Insulin **glargine** is a newer synthetic insulin analogue, currently only licensed for use in humans, and so can only be used off license in cats if the veterinary licensed formulations have proven to be inappropriate. This insulin forms microprecipitates at the site of injection meaning that small amounts of insulin are slowly released. This produces a fairly constant serum concentration of insulin over 24 hours rather than having a peak

concentration. Glargine is still undergoing assessment in diabetic cats, but may be particularly of use in those cats where Caninsulin has a short duration of effect. There are specific guidelines available for using glargine and it is important that these are followed closely. **In the UK Caninsulin would have to be shown to be ineffective to allow use according to the cascade – this is rare so experience with Glargine in the UK is limited. Studies show that twice daily Caninsulin is very effective at producing remission (28% in one study – Martin and Rand 2007) and control of clinical signs.**

- Caninsulin has a duration of action of around 8 – 12 hours and a nadir of around 4 hours

### The new diabetic

- Evaluate the cat for concurrent diseases with minimum database of CBC, biochem and UA (inc. culture or at least sediment exam)
  - Arrange long consult with owner plus nurse to demonstrate injections
  - Start on ~0.25 IU caninsulin/kg/per injection (to a maximum of 3 IU/cat), twice daily
  - On day one hospitalise the cat and check blood glucose at the estimated nadir (e.g. 4-8 hours after administration) to ensure no hypoglycaemia. As long as blood glucose is not below 10 mmol/l continue on the same dose
  - Discharge the cat for one week with instructions for the owner on monitoring for hypoglycaemia. No changes to the dose of insulin should be made during this time. This is because it takes at least 3-4 days for glucose homeostasis to adjust after starting or altering insulin doses.
  - During this time the owners can also monitor urine ketones at home and should contact the veterinary practice if ketones become positive, and they should also monitor for signs of hypoglycaemia **do not allow owners to measure urine glucose!** They may overinterpret the results.
  - Ensure owners inject at alternate sites to reduce the effect of reduce absorption.
  - After a week the cat can be hospitalized for around 12 hours, and measure BG every 2 hours – this is to assess response around the nadir and if there is not a significant response to insulin then there is little value in testing more frequently than 4 hourly at this stage
  - The aim of a blood glucose curve at this stage is to ensure no periods of hypoglycaemia, to assess if there is any response to that dose, and if so roughly when the nadir (time of peak action of insulin, the lowest point of the curve) is occurring. The nadir can be difficult to predict since there is a wide variation in the duration of action of the different insulins between different cats, so the nadir always needs to be determined in the individual
  - If there is no reduction in BG increase insulin dose by a total (and maximum) of 0.5 units per injection
  - Once the nadir BG is 8 – 13 mmol/l consider performing a more complete BG curve
- NB There is no value in performing a complete BG curve if the cat is receiving a dose of insulin that is not having a significant effect on BG concentrations since the nadir and duration of effect will be impossible to evaluate.

## Performing & interpreting blood glucose curves

- ***Think about using the ears (see below) rather than the jugular to avoid stress and destroying the veins***
- The aim of a BGC is to identify BG concentration at the nadir, obtain a more precise time for the nadir, evaluate the duration of effect of the insulin and ensure Somogyi overswing is not occurring. Once these details have been identified, subsequent BG curves may only require every 4 hourly sampling, particularly if the cat is clinically stable
- A BGC is performed by checking the cat's blood glucose concentration, then giving it its usual breakfast and dose of insulin, then determining its blood glucose level every 1-2h during a 12-24h period. 12 hours may be sufficient if BG has increased back to its pre-insulin concentration after 12 hours, but if it hasn't the curve should be continued for 24 hours. If the level of the blood glucose at its nadir (lowest point) is not adequate then the dose of insulin may need to be increased. If the duration of action is too short then it may be required to change to a longer acting insulin (e.g. PZI or glargine), or switch from once or twice daily administration. After recommending the change the cat should be discharged on the new regime and the whole process repeated after a further seven days. Only one change to the insulin regime should be made at one time.
- Ideally blood glucose concentration should be maintained between 5 -14 mmol/l

### ***The stressed cat***

In a highly stressed cat BGC can be useless. Studies demonstrate a big difference in results at home compared to those at the clinic. It is meaningless to do a long BGC in a stressed out cat. So in these cases consider:

- Using clinical signs and fructosamine
- Perform 'mini curves' to avoid hypos just measure for 3-4 hrs around the nadir and then use clinical signs and fructosamine

#### **How to perform ear tip blood glucose measurements**

- A warm swab is held over the peripheral ear vein to help dilate the peripheral muscles
- The edge of the ear is smeared with Vaseline to prevent the blood running into the hair coat
- The ear is then held firmly and gently between four fingers, which act in pairs to raise the vein and prevent its movement
- The vein can then be piced using either a fine hypodermic needle or a lancet. Holding the vein still for a few seconds will allow a bleb of blood to form
- This can then be transferred to the glucometer test strip or, where appropriate, the glucometer can be applied directly to it.

- BCGs can provide very useful information but studies have shown that BGCs in an individual cat will vary widely from day to day. It is therefore very important that major changes to treatment are not based on a single blood glucose curve. All BCGs need to be interpreted in conjunction with the cat's clinical status, fructosamine results and the environment in which the cat was in when the curve was performed. The most important aspect to consider with BCG results is *trends* of change, so comparing previous BCG results is an important part of interpretation. Rather than thinking of a BGC over a 24 hour period, it is useful to think of a BGC over a week and aim to try and keep the BGC consistent from week to week (i.e. monitoring trends), but accepting daily fluctuations are a normal occurrence.

### **Dietary therapy: important points**

- High fibre, moderately fat restricted diets are usually successful weight loss diets for obese cats
- High protein and low carbohydrate diets are recommended for diabetic cats of any body weight and can also be used as a weight loss diet
- Feeding a high protein and low carbohydrate diet will result in better glycaemic control and increase the chance of being able to discontinue exogenous insulin
- Dry foods tend to contain much higher proportions of carbohydrate compared to wet foods, so a wet diet is preferable where possible
- If prescription diets are not an option, look for supermarket diets with the lowest carbohydrate and highest protein proportions
- Ad-lib feeding is acceptable as cats do not develop significant post-prandial hyperglycaemia
- Administering insulin during or after feeding is most practical, to ensure that the cat is eating before insulin is given
- Cats that are fed ad lib and 'graze' their food throughout the day and/or night should continue this regime providing they are not gaining weight. Cats that eat their food all at once should be given 2 meals (half of total calorie intake at each meal, at the time of insulin injections if on twice daily insulin treatment). Consistency with the chosen feeding regime, and monitoring amount of food eaten daily are most important
- Also consider concurrent disease with dietary choice e.g. if CKD is also present, a diet with lower protein content may be considered

### **Which diet to choose?**

High fibre, moderately fat restricted diets are usually successful weight loss diets and have been previously shown to improve glycaemic control in diabetic cats. However these high insoluble fibre diets are less palatable and may result in inappetence in some cats, in addition



to larger faecal volume and subsequent risk of constipation in some individuals. Cats have a high dietary protein requirement and use amino acids and fat for energy, rather than carbohydrates. ***High carbohydrate diets increase the risk of obesity in cats, and in diabetic cats predispose them to higher postprandial blood glucose concentrations.*** More recently therefore, high protein and low carbohydrate diets have been developed for diabetic cats and have proved to have a significant effect on improving glycaemic control and there has even been resolution of the insulin dependent state in some diabetic cats.

**Consider high protein – low carbohydrate diets for diabetic cats!**

**Weight loss programmes for obese cats -**

<http://www.catprofessional.com/overweight.html>

Below is an article/notes on feline obesity as it is so linked with DM I thought it might come in useful!

Obesity is defined as the accumulation of excessive adipose tissue, with obese cats 20% or more above ideal body weight. Overweight pets are 10-19% above this optimal weight. It is often reported in the press that humans are getting bigger each year and an 'obesity epidemic' is upon us. This is an area where our companion animals are following their owners and as vets we are seeing more and more overweight and obese dogs and cats. Several studies have looked at this issue in dogs over the last few years and the problem in cats is now also well recognised, although less well studied. This article will discuss why our cats are getting fatter, the associated health problems, how we should manage these challenging patients, and how to prevent the weight gain in the first place.

### **Why are we seeing more fat cats?**

The prevalence of overweight or obese cats in the UK varies between 18% and 52%, depending on the study, and risk factors identified include neutering, inactivity, ad-lib feeding, frequent feeding and middle age. Some of these seem obvious but to get to the bottom of it we need to look at the natural feeding behaviour of cats and what has changed in our management of this species over the last 10-20 years.

A cat's natural feeding behaviour includes the consumption of a high protein diet consisting of multiple small meals (usually rodents/birds). Hunting behaviour expends a large amount of energy and in the past many cats were kept exclusively outdoors and not neutered. The modern pet cat is a very different feline. This cat is neutered and provided with often a lower protein/higher carbohydrate diet which is consumed without any energy expenditure. Many cats are fed a constant supply of food and some are kept entirely indoors. Neutering is an important risk factor for obesity, likely mainly due to a reduction in activity as well as a possible effect on metabolic rate. This of course does not mean neutering should not be encouraged, as the benefits far outweigh these risks, but it does mean that attention should be paid to diet and activity following neutering and owners made aware of the risk and a plan made for regular re-assessment of body condition score (see below, prevention of obesity). Misinterpretations of behaviour also play a role in over-feeding of cats. Cats are not social eaters and do not need contact with owners around feeding time, but often when a cat initiates contact by rubbing the owner's legs or purring, the cat is assumed to be hungry and is fed, quickly learning to prompt their owners to provide food. Anxiety disorders are

recognised in cats and over-eating can be a behavioural problem. Clearly the manipulation of the feline species into sedentary pets has resulted in a new generation of overweight cats.

### **Recognition of obesity and recording of body weight and condition score**

A physical examination, done for whatever reason, should include measurement and recording of body weight. This allows comparisons to be made at subsequent visits and can identify 'at risk' cats, particularly neutered young adults who gain small amounts of weight each year and become overweight at middle age. However, body condition score (BCS) should also be measured as obviously ideal weight will vary between different size cats. This can also be done by owners at home and identify problems early. Several scales and guides are available using either a 5 or 9 point score, or by measuring ribcage circumference and are available via pet food companies. Other scales also include an assessment of physical health. Ideally the same scale/system is used by all vets within a practice so a quick check on the records can indicate if a cat's BCS is too high or has changed. Once an overweight or obese cat is identified the practice should have a system in place to provide a treatment plan along with advice and support for owners.

### **Management of overweight cats within the veterinary practice – how to make the fat cat slim**

Management of the overweight cat should be approached from 2 sides: dietary management and lifestyle changes/increasing the cat's activity. What support/follow up can be provided to the client should also be considered.

#### **1. Dietary management**

This aspect is obviously the mainstay of weight control and should begin with an assessment of current food intake. A 'food diary' is a good way to do this and should include the following: type of food given, how much food is given, how it is provided and any treats or human food (including milk). Once current food intake has been established a weight loss plan can be created considering: ideal and target/goal weights, type of food, how much food to feed and how to provide the food.

- **Ideal and target/goal weights:** an 'ideal weight' can be approximated from assessment of body size and current condition score. Generally the cat's weight at maturity as a young adult is an ideal weight, before excessive weight gain began. This weight may be a long way from the current weight and seem unrealistic to owners. Therefore 'target or goal weights' are set along the way. These are achievable goals, based on monthly weight loss, and when one is reached another is set until the ideal weight is reached. **Overweight or obese cats should not lose more than 1% of body weight per week.** Any quicker and complications such as hepatic lipidosis are risked.
- **Type of food:** there are many diets available from different manufacturers and an obese cat will in most cases lose weight most effectively using a prescription diet. Overweight cats may be managed using the current diet with revision of amount fed and reduction of treats. Again the food diary is useful here as it will identify areas of over-feeding. High protein/low carbohydrate diets are suitable for weight loss and generally more palatable than higher fibre/low fat diets. Dry food contains more calories per gram than wet food, and more carbohydrate, so a change to a wet diet can be beneficial (particularly in cats with lower urinary tract disease). Cats can lose weight successfully on a dry diet

but owners must weigh the food and recognise that the amount fed may look smaller. Kibbles are certainly easier to provide in different ways to increase activity (see later).

- **Amount of food:** clients should be encouraged to weigh the food as a little extra each meal adds up. Clients should be guided on the correct amount to feed according to the box below:

#### Calorie counting for cats

- Calories needed to maintain an ideal body weight can be calculated as follows:  
**Calories per day (kcal) = (30 x ideal body weight in kg) + 70**
- An overweight/obese cat is then fed 60-70% of this amount in order to lose weight
- This can represent too rapid a drop in calorie intake for cats that are being severely overfed and therefore calculating current calorie intake from a food diary may allow a more gradual reduction towards the ideal amount (and feel more realistic to the client)
- The calories in various cat foods may not always be stated on the packaging but can be obtained from the manufacturer and feeding guides are often available on prescription weight loss diets
- Treats must be taken into account and can be taken out of the daily calorie allowance

- **How food is provided:** mimicking a cat's natural feeding behaviour can encourage energy expenditure, and relieve boredom in indoor cats. This can be done by using treat balls or homemade puzzle feeders (see picture), placing food (kibbles) in different locations in the house (on each level, on scratching posts etc) and using a feed timer to open during the working day providing small, more frequent meals.

## 2. Increasing activity

Weight loss is more successful if combined with an increase in activity. Many overweight cats are sedentary and getting them moving improves their quality of life significantly. See the box below and <http://indoorpet.osu.edu/index.cfm> for more information and ideas.

#### **Tips for increasing activity in overweight cats**

- Encourage owners to play with their cats – even 5 minutes a day with a fishing toy can help (see picture)
- Toys can be provided to encourage play, catnip toys are popular, but simple rolled up balls of paper or a ping pong ball in the bath can be fun for cats
- Indoor cats need their owners to make efforts to enrich their environment and encourage activity; outdoor access into a 'cat proof' garden or enclosure are good ideas but if not possible then scratching posts and climbing frames should be provided
- Osteoarthritis is common in older cats which will of course be reluctant to move, and in a vicious cycle being overweight can then worsen osteoarthritis. Affected cats may need analgesia to get them moving and help weight loss. Often analgesics can be withdrawn once an ideal weight is reached

### **3. Support provided by the practice**

Once a weight problem has been identified the client should be referred to a practice member who can help assess the case and formulate a weight loss plan. During a 10 minute consultation (often for a condition other than the cat's weight) it is very difficult to adequately discuss weight loss techniques. A motivated vet or nurse can play the role of the practice's 'weight loss expert' and consult with the client by phone or preferably during a face to face consultation. This is where 'weight-loss clinics' can be invaluable (see box). Consider also providing printed literature and support materials for the client.

#### **Weight loss clinics – why they work AND benefit the practice**

- Weight loss in cats can, and should, be a slow process during which clients may lose motivation and need regular meetings to assess progress and provide advice and encouragement
- Clients are more likely to be successful sticking to a diet if supported
- Rapid weight loss may result in complications such as hepatic lipidosis so cats should be weighed every 1-2 weeks initially, then monthly to ensure weight loss does not exceed 1% of body weight per week
- Hiccups and problems are often encountered during a weight loss program – early identification can avoid clients losing faith and giving up
- Health problems may develop during the program that are identified at clinic visits
- Clients appreciate this service and attention and are more likely to stick to a weight loss plan and remain loyal to the practice

### **Prevention of obesity – how do we educate our clients?**

As mentioned previously recording of body weight and condition score from a young age is helpful in identifying the cats that need attention paid to their diet to avoid ongoing weight gain. Vaccination appointments are an opportunity to talk about diet/activity but checking a middle aged cat's weight every 6 months may be better, this can be done in a nurse's clinic, along with routine health checks such as blood pressure.

Owners of 'at risk' cats should be informed how to avoid excessive weight gain. Neutering is a known risk factor and therefore providing owners with dietary advice/printed literature at neutering and arranging a re-check appointment 6 months later makes sense (remember this is also a time cats are often lost to a practice). As cats approach middle age their risk of obesity increases so providing owner of cats of this age group with information, via a practice leaflet or mail-shot may encourage owners to seek further advice.

Weight gain is not always considered a medical problem, but we now know that it is associated with avoidable complications and a reduction in quality (and probably length) of life and as such it's management should be a practice priority.

#### **References and further information:**

Scarlett J, Donoghue S. (1998) Association between body condition and disease in cats. *J Am Vet Med Assoc* 212:1725-31.

Courcier EA, O'Higgins et al (2010) Prevalence and risk factors for feline obesity in a first opinion practice in Glasgow, Scotland. *J Fel Med Surg* 12:746-753

See the International Society of Feline Medicine/Feline Advisory Bureau's Well Cat and Cat Friendly Practice initiative for more information on lifestage clinics and preventative healthcare: [http://www.fabcats.org/well\\_cat/for\\_life/index.php](http://www.fabcats.org/well_cat/for_life/index.php), <http://www.isfm.net>

#### ***Monitoring diabetic control***

*It is easy to get caught up thinking about blood glucose curve but other factors are more important such as owner's feelings on how things are going and clinical signs. So the following are monitoring tools.*

1. Clinical signs – owners should be encouraged to keep a diary including demeanour, appetite, thirst, urination (just approximately to get an idea of PU/PD). Also make sure owners go home with information on the signs of hypoglycaemia.
2. Serum *fructosamine* concentrations. This can be done monthly during the initial months of stabilisation
3. *Blood glucose curves* – as explained above, caution needs to be taken when interpreting BGC results
4. *Regular clinical exams* – to also look for complications, weight loss/gain, other diseases developing, coat condition etc
5. *Further testing* – ideally once stable diabetic cats are re-examined every 3-6 months and have as well as a physical exam, weighing and fructosamine, a biochem/urinalysis and haematology performed. This older patient group will develop other diseases as they get older!

In the longer term, once stabilized, diabetic cats should be reassessed at least every 3-6 months.

**A note on urine dipstick testing at home**

This is generally a bad idea as owners may then decide to alter insulin without consulting you plus the amount of glucose in the urine is affected by SG, time between urination etc etc

There are a few exceptions – identification of ketonuria is obviously a cause for concern. So periodic dipping by owners for this complications, particularly at the start of treatment might be a good idea

Dipping periodically may also identify the absence of glucose consistent with hypoglycaemia or resolution of transient DM and prompt a BGC or fructosamine assessment

***The transient diabetic***

The risk with these cats is the development of hypoglycaemia. This is why home glucose monitoring can be useful to identify a low BG prior to insulin administration. This can happen as an inciting factor resolves (e.g. pancreatitis settles down). You may note with these cats as the insulin requirement decreases:

- Low BG (<10mmol/l) prior to insulin administration
- Low/normal fructosamine concentration
- Persistent absence of glucosuria – home monitoring of urine glucose is not a good idea/reflection of glycaemic control BUT in this situation identification of a NEGATIVE urine glucose is helpful!

**The difficult diabetic**

It is not uncommon for problems to be seen in the early stages of care of the diabetic at home.

There are many causes of diabetic instability – see the box below:

## **Causes of Diabetic Instability in Cats**

### **Insulin Factors**

Handling -	Freezing, overheating Violent agitation of the bottle Expired insulin
Choice of insulin -	Inappropriate duration of action Inappropriate species of origin
Dosing regimen -	Inappropriate dosage interval
Administration Problems -	Poor injection technique Poor absorption from injection site Inaccurate dosage Incorrect syringe for insulin type

### **Monitoring and Dosage**

Inappropriate monitoring -	Effects of stress Using single blood glucose measurements Somogyi overswing
Dose adjustments -	Too frequent dose increases Too large dose increases (>20%)

### **Cat Factors**

Stress	
Underlying disease -	Inflammatory conditions <ul style="list-style-type: none"><li>• Pancreatitis (particularly important cause)</li><li>• Inflammatory bowel disease</li><li>• Respiratory disease</li></ul> Infectious disease <ul style="list-style-type: none"><li>• Urinary tract infections (can be occult)</li><li>• Dental disease</li><li>• Viral infection (FIV, FeLV)</li></ul> Renal insufficiency/failure Hepatic disease Hypertension Cardiac disease Hyperthyroidism Hyperadrenocorticism (note uncommon cause) Acromegaly (note uncommon cause)
Treatment with corticosteroids or progestogens	

The first thing that should be done when there are any problems with stabilisation is to ask the owner to demonstrate how they mix and inject insulin in order to check that this is being done correctly. In some cases it will be necessary to re-admit the cat for more detailed assessment which may include a 24 hour glucose curve.

Of the above causes in the box some need special mention:

- Pancreatitis – over 50% of diabetic cats are likely to have pancreatitis. Cause and effect is difficult to establish but the presence of pancreatitis often results in very variable insulin requirements. Chronic pancreatitis can be difficult to diagnose and cats may show few clinical signs associated with it. Measurement of fPLI is the most sensitive test available for diagnosing pancreatitis, but even that is not 100% sensitive so a normal fPLI does not exclude pancreatitis. Achieving a diagnosis of pancreatitis is unlikely to alter the way a

cat's diabetes mellitus is treated, and treatment for the pancreatitis itself is merely symptomatic, however it provides some explanation as to why a cat may have extremely variable insulin requirements. These cats can be very difficult to control.

- Infections – any infection – UTI, particularly but also dental disease will cause problems with stabilisation and need identification and treatment
- The odd conditions – acromegaly and hyperadrenocorticism are rare in cats and not the most common cause of instability – rule out the common before jumping to the uncommon! However, the most common presenting signs of these conditions is uncontrolled DM.

### **Commonly encountered problems**

#### ***Hypoglycaemia***

Hypoglycaemia can be a common complication of insulin treatment, arising in a number of ways e.g. the insulin dose is increased too rapidly (particularly if stress hyperglycaemia is mistaken for poor glycaemic control), if a previous insulin resistance has resolved, and if a cat has reverted to a non-insulin dependent state.

It is important to be aware that hypoglycaemia can be difficult to recognise early in cats, as in contrast to dogs, cats do not always exhibit polyphagia when they become hypoglycaemic. The earliest sign that owners often note is that the cat goes and hides more than usual.

If hypoglycaemia occurs, insulin should be discontinued until hyperglycaemia recurs and then reinstigated at half of the previous dose. If blood glucose levels are still low or normal when the cat is receiving 1 unit or less of insulin, then resolution of the insulin dependant state should be suspected.

#### ***Somogyi overswing***

This describes a normal physiological response to hypoglycaemia induced by excessive insulin administration. This commonly occurs when insulin doses are increased too quickly with inadequate monitoring, or if the cat has very fluctuating insulin requirements. When blood glucose concentrations reduce below 3.5 mmol/l or when they fall very rapidly, counter-regulatory hormones such as glucagon and adrenaline are secreted, resulting in a rebound hyperglycaemia and insulin resistance within a few hours. This hyperglycaemia persists for at least 24 hours in most cases, and can last for up to 72 hours, or occasionally even longer. Clinical signs of hypoglycaemia are rarely seen, and therefore the cat will present as not responding to insulin. The speed of reduction in blood glucose is often the trigger for Somogyi overswing, so overt hypoglycaemia may not be present. The overswing can occur very rapidly following injection and requires ½ -1 hourly BG measurements following insulin administration



to be detected. Insulin should be withdrawn for 3 days prior to this to ensure that any rebound hyperglycaemia has resolved. If the Somogyi phenomenon is not recognised, insulin doses are further increased, resulting in even more severe rebound hyperglycaemia. Diagnosis is made by demonstrating hypoglycaemia or a rapid fall (e.g.  $> \sim 10\text{mmol/l}$  in one hour) in blood glucose, but can be missed if blood samples are taken less frequently than every hour following insulin administration. Furthermore, reduction in blood glucose will not always be evident if the subsequent rebound hyperglycaemia and insulin resistance lasts for more than 24 hours. In addition, serum fructosamine may be elevated if rebound hyperglycaemia is prolonged. If there is a possibility of overswing occurring it is advisable to reduce the insulin dose to 0.25 - 0.5 IU/kg for a few days and assess the cat's response. In the short term, hyperglycaemia is a "safer" state than insulin induced hypoglycaemia. If no improvement in clinical signs are observed, and no reduction in blood glucose demonstrated, then another cause of insulin resistance should be considered.

### ***Fluctuating insulin requirements***

It is not unusual for some cats to have very fluctuating insulin requirements, with uncontrolled diabetes one moment and then development of hypoglycaemia the next. The most usual reason for this is the development of a concurrent disease that causes a mild insulin resistance that later resolves spontaneously, or waxes and wanes. Inflammatory diseases such as chronic pancreatitis are commonly associated with these fluctuating requirements. These cases can be extremely difficult to manage, and this is one situation where home blood glucose monitoring can be very useful.