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Interesting facts from the Laboklin expert round table on the topic of hypothyroidism

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Hypothyroidism is a common endocrine disease in dogs. As an aid we have summarised important aspects of this disease from a recent expert round table discussion on the subject of hypothyroidism.

Participants of the expert round table were: Dr Astrid Wehner, Dipl. ECVIM-CA (Head of the Endocrinology Department, Medical Small Animal Clinic, LMU Munich), Dr Florian Zeugswetter (Head of the Endocrinology Department, University Hospital for Small Animals Vienna), Alenka Hrovat, PhD, Dipl. ECVIM-CA (Pride Veterinary Center, University of Nottingham, UK) – who has published on the relationship between behavioural changes and hypothyroidism, Prof. Andrea Fischer, Dipl. ECVN, Dipl. ACVIM (Head of the Department of Neurology, Medical Small Animal Clinic, LMU Munich) – who deals with the relationship of hypothyroidism and neurological symptoms and Prof. Wolfgang Bäumer, Dipl. ECVPT (Institute of Pharmacology and Toxicology, Department of Veterinary Medicine, FU Berlin) – who is a member of the Federal Veterinary Association Committee for Medicinal Products and Animal Feed Law.

Is this hypothyroidism or not?

A low serum T4 concentration does not necessarily equate to hypothyroidism. In particular, other diseases can lead to reductions. How can such a low value be checked to determine whether it actually indicates hypothyroidism or is merely reduced due to another, non-thyroidal disease?

Dr Astrid Wehner highlights the value of the **clinical examination**. If the dog does not show a typical clinical sign such as weight gain with normal feed intake and reduced performance, and if the general examination does not reveal classic changes such

as thickened skin, poor coat quality, and possibly also alopecia, scepticism is indicated.

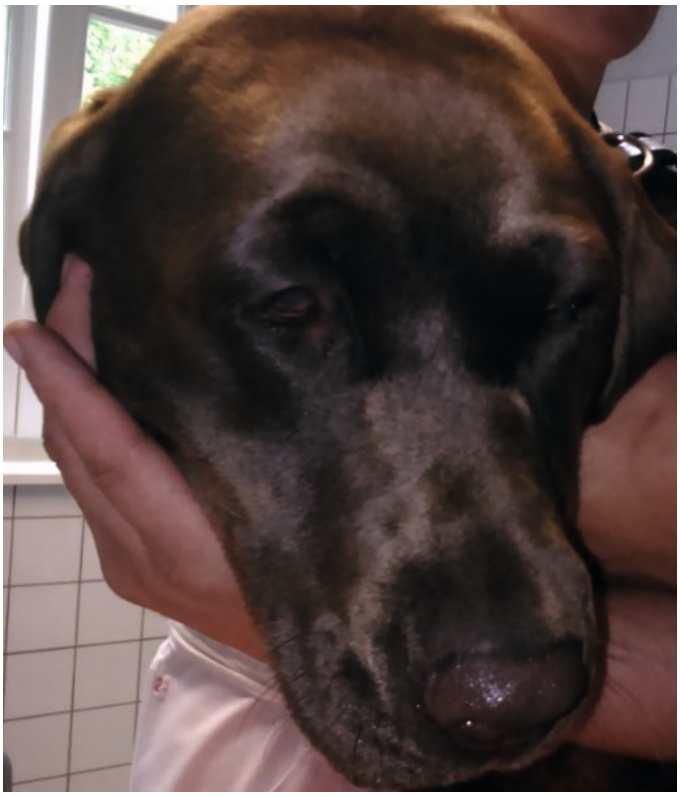

Fig. 1: Myxedema and coat discoloration in a dog with hypothyroidism *Image source: Dr Jennifer von Luckner*

Dr Florian Zeugswetter confirms that a **complete thyroid profile** can help shed light on the subject. In particular, the combination of T4 and TSH is known to be extremely valuable. If T4 is low while TSH is elevated, we can be relatively certain that hypothyroidism is present. Unfortunately, in about 30 % of hypothyroid dogs, TSH is within the normal ranges.

Thyroglobulin antibodies (ATG) can also provide guidance. If they are positive, thyroid pathology is present and, in borderline cases, may reinforce the suspicion of hypothyroidism. However, this does not automatically mean hypothyroidism is present. Many dogs develop antibodies to thyroglobulin, T4, or T3 during their lifetime, but only a relatively small percentage subsequently develop hypothyroidism. However, knowledge of antibodies has another significance: T4 concentrations can be falsified by interference with antibodies. Not only a falsely high but also a falsely low measurement is possible. Thus, caution should be exercised in interpreting T4 concentrations when ATG are detected.

Naturally, the question about the value of measuring free T4 (fT4) followed. Dr Florian Zeugswetter points out the difference between the different measurement methods. The gold standard is still the so-called equilibrium dialysis with subsequent determination of the filtered fT4 by radioimmunoassay (RIA). FT4 measured with this method is less influenced by non-thyroidal diseases than total T4. This is only partially true for fT4 determined by other methods. Since the dialysis RIA technique is now only offered by a few laboratories in the USA, we usually have to make do with the values determined by so-called CLIA methods. We should bear in mind that these values are also influenced by other diseases and medications.

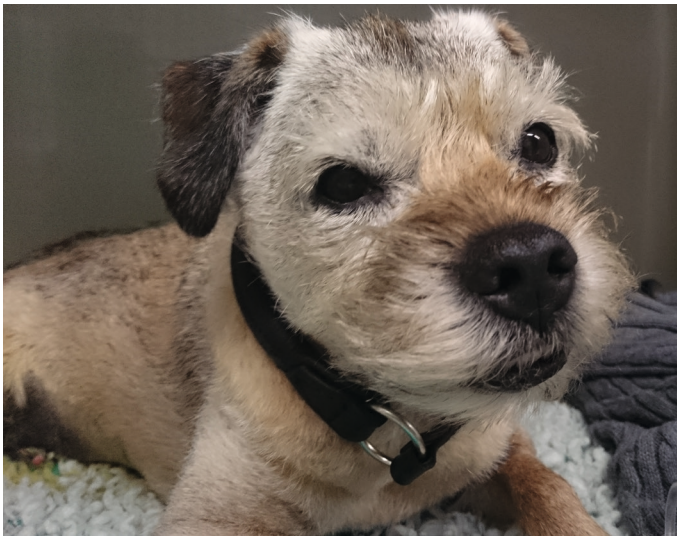

Fig. 2: Border Terrier with hypothyroidism and mucocele – a common combination in this breed
Image source: Dr Jennifer von Luckner

In this context, a discussion arose regarding **influencing drugs**. Such drugs are e.g., glucocorticoids as well as anticonvulsants like phenobarbital.

Prof. Andrea Fischer explains that we are facing big problems especially with phenobarbital. Dogs treated with phenobarbital are often clinically as sluggish as hypothyroid patients. Phenobarbital reduces T4 and can even increase the TSH concentration (but usually only within the reference interval).

Optimally, a functional test is carried out in such patients.

It is known that the TSH stimulation test is very reliable, but unfortunately too expensive for routine use. Scintigraphy is only possible in specialised centres.

Dr Astrid Wehner reports that a reinterpretation of the inexpensive and easy-to-perform TRH test was reviewed at Utrecht University. In the study, a minimum 57 % increase in TSH 45 minutes after injection of TRH (10 ug/kg i.v.) proved a physiological function of the thyroid gland, whereas the TSH increase was lower in hypothyroid dogs. Clinical experience is still lacking to confirm these results for everyday practice. However, the panel agreed that the test appears to be very useful. Alenka Hrovat points to the **therapy test** as a valid possibility in practice. However, this should not only be done on the basis of a low T4 concentration, but only if there is a well-founded suspicion.

Dr Florian Zeugswetter interjects that especially in dogs with behavioural problems it has to be taken into account that thyroxine is a psychotropic agent. Regardless of hypothyroidism-induced signs, administration will lead to behavioural changes. Interestingly, this can also be the reduction of activity, which can lead to misinterpretation in hyperactive/anxious young dogs.

Can young dogs have hypothyroidism?

Dr Astrid Wehner considers the relatively common practice of supplementing young dogs with behavioural problems with thyroid hormones, who do not show classic signs of hypothyroidism and whose T4 concentrations are usually in the normal range, to be problematic. If a young dog shows no TSH elevation, hypothyroidism is unlikely. An isolated low T4 concentration in young dogs is highly suspicious for non-thyroidal disease.

Subclinical hypothyroidism is defined as a TSH elevation with still normal T4 concentration and thus represents an early stage of thyroid disease. There are usually no signs at this stage (hence the term "subclinical"). Monitoring should be done to distinguish dogs that develop clinical hypothyroidism from those that remain euthyroid. Unfortunately, the term is often misused to describe animals that suffer from behavioural abnormalities and have normal TSH and T4 concentrations.

There are predisposed breeds, such as Rhodesian Ridgeback or Golden Retriever, and it is possible for hypothyroidism to develop at a young age. However, these dogs should fulfil the classic diagnostic criteria (of compatible clinical signs, low T4, and elevated TSH).

Alenka Hrovat also fears that many young dogs with behavioural problems are supplemented with thyroid hormones without justification. Scientifically, it has not yet been proven that fearfulness or aggressiveness are linked to hypothyroidism.

The many faces of hypothyroidism

Prof. Andrea Fischer is of a similar opinion and points out that it is rather other symptom complexes from neurology where hypothyroidism can play a role as an immune-mediated concomitant disease or cause of muscle weakness. Examples are myopathy, polyneuropathy, myasthenia gravis, laryngeal paralysis, facial nerve palsy, megaoesophagus and very rarely vestibular syndrome. In addition, hypothyroidism can be a possible cause of an infarction (stroke).

The treatment

There is uncertainty about the new pharmaceutical act and how to deal with the manufacturer's instructions. What to do when one manufacturer gives a once-daily dosage and the other a twice-daily dosage?

Prof. Wolfgang Bäumer can reassure us regarding this. As long as a dosage recommendation and not an explicit dosage specification is given in the package insert, we veterinarians are not bound by it. The preparations can be given **once or twice** a day regardless of the manufacturer's recommendation.

The question arises whether the preparations for the different claims made by the manufacturer differ in their pharmacokinetics?

In this context, Prof. Wolfgang Bäumer explains that this does not have to be the case. Due to the relatively short half-life of thyroxine, twice-daily administration seems to make sense from a pharmacological point of view. At the same time, clinical signs can certainly be remedied in many

cases with once-daily administration. It is interesting to note, however, that in human medicine there is a debate about avoiding changing preparations during treatment as much as possible.
Dr Florian Zeugswetter always gives thyroid hormones on an **empty stomach**. He is convinced that otherwise they are not sufficiently absorbed. Prof. Wolfgang Bäumer confirms in principle that absorption is better when the patient is fasting, but points out that there could be individual variations depending on the dog. Alenka Hrovat notes that the compliance of dog and owner is better when medication is given with food. She therefore prefers this variant and has few problems with the setting in everyday clinical practice. All experts agree that the chosen scheme must be maintained on the day of blood collection for monitoring.

What is the legal situation regarding long-term medication?

Prof. Wolfgang Bäumer points out that even a patient on a long-term medication must regularly come in for a clinical examination. What exactly is meant by "regularly", however, is not clearly defined in the Veterinary Medicines Act. However, a corresponding presentation should be documented at least every 3 months.

Unfortunately, sending medication by post is not permitted even in the case of long-term medication!

Also, the medication may not be administered on behalf of another colleague (e.g. if the owners have forgotten the tablets on holiday) without examining the dog. However, verification of the diagnosis by requesting the thyroid findings is not mandatory.

Monitoring

What if the T4 concentration does not increase under substitution?

Dr Astrid Wehner strongly advises to take another look at the diagnosis in such a case. Was a nonthyroidal disease overlooked? Such diseases may have led to a misdiagnosis. It is also possible that other diseases exist in addition to hypothyroidism, making the diagnosis difficult. A similar problem can occur with interference from certain medications. In addition, medications that inhibit stomach acid formation or contain calcium reduce thyroxine absorbtion, which applies to food present in the stomach.

Prof. Wolfgang Bäumer points out that from a pharmacological point of view, the time interval between tablet administration should be observed. If the time interval of 4 – 6 hours after tablet administration is exceeded, the T4 concentration will already drop significantly again.

Alenka Hrovat reminds us that the **target range for T4 should be in the upper reference range**.

Dr Florian Zeugswetter can tell us about the additional determination of TSH and/or thyroglobulin antibodies as part of the monitoring. A TSH measurement to **check the sucess of the therapy**, makes sense, if the TSH was elevated at the time of initial diagnosis. A TSH concentration in the reference range should be aimed for. The decrease in thyroglobulin antibodies during therapy has no significance with regard to the success of the therapy. However, it should be noted that the antibodies can falsify the T4 concentrations. This can play a role if the laboratory result and the clinical condition of the patient differ. Dogs with autoantibodies usually do not need more L-thyroxine than other patients!

Dr Jennifer von Luckner