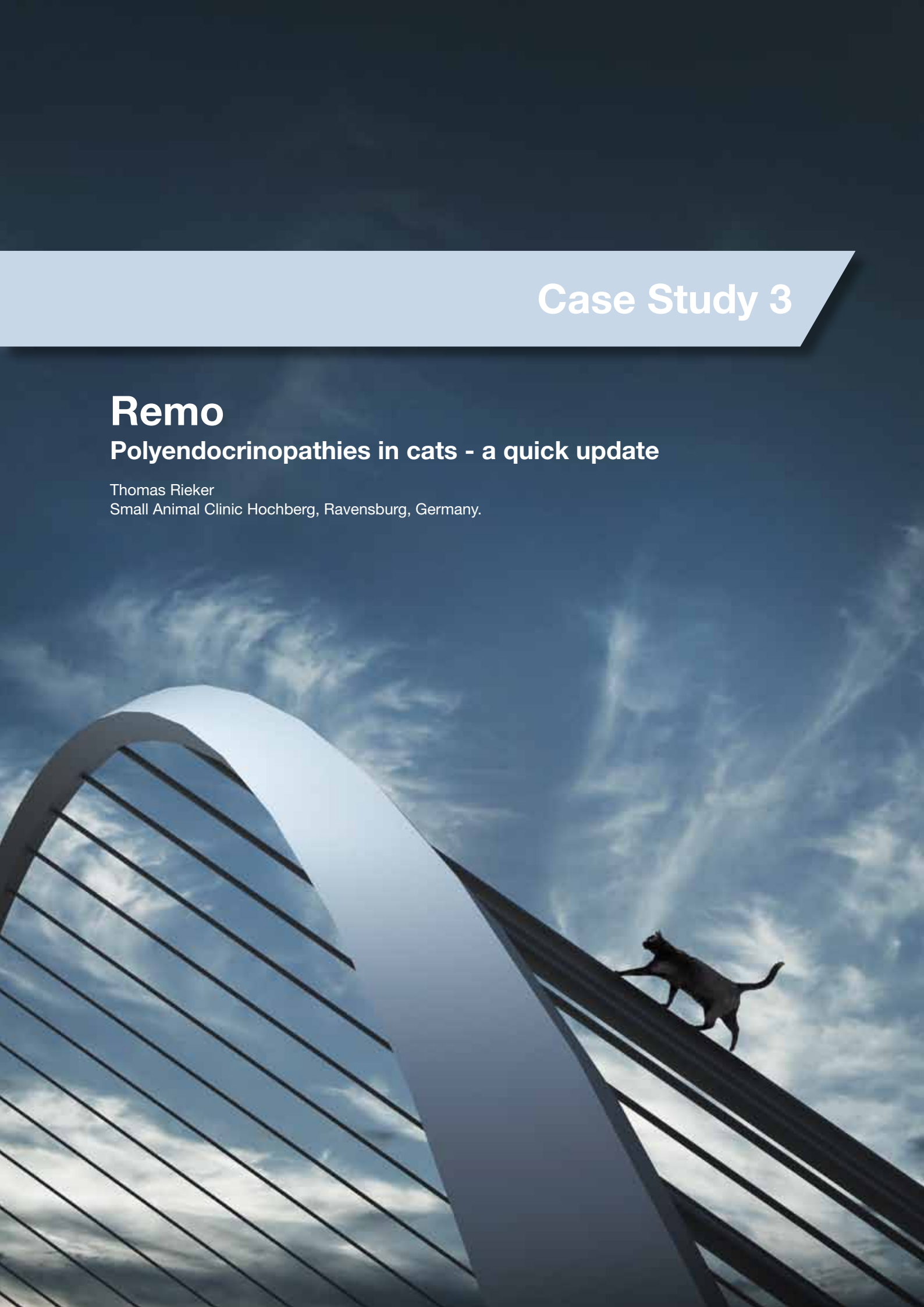


## Case Study 3

# Remo

## Polyendocrinopathies in cats - a quick update

Thomas Rieker  
Small Animal Clinic Hochberg, Ravensburg, Germany.



**In humans, polyendocrinopathies are a well-known syndrome, which is mostly attributable to genetic and autoimmune causes. Do polyendocrinopathies play a role in cats? What are the most common simultaneously occurring feline endocrine disorders? Is there a pathophysiological link between the various feline endocrinopathies? What should be taken into account in diagnostics?**

**Before we address these issues, let's first look at a specific clinical case:**



**Signalment:**

Remo, a European short-haired, 12-year old castrated tomcat, who is free to roam outdoors and whose current bodyweight is 4.8 kg.

**History:**

Very clear weight loss over last few weeks, even though appetite was maintained and even increased, polyuria/polydipsia, occasional diarrhoea, fed with premium dry feed.

**Clinical examination:**

- hands off: Body condition score index 4/9, unkempt coat, respiratory frequency 28/min
- hands on: Thyroid easily palpable, mucous membranes pale pink, capillary refill time approx. 1s, skin fold disappeared immediately, deep abdominal palpation soft stomach, pulse powerful, heart frequency 144/min.

**Lab Tests:**

| Test                   | Result | Normal value | Unit   |
|------------------------|--------|--------------|--------|
| T4 (basal value)       | 123.6  | 10 - 60      | nmol/l |
| BUN                    | 11.6   | 5.7 - 13.5   | mmol/l |
| Creatinine             | 74     | < 168        | µmol/l |
| Sodium                 | 157    | 149 - 163    | mmol/l |
| Potassium              | 3.4    | 3.3 - 5.8    | mmol/l |
| Inorganic phosphate    | 2.3    | 0.8 - 2.2    | mmol/l |
| Bilirubin              | 2.6    | < 5.1        | µmol/l |
| ALT (GPT)              | 352    | < 175        | U/l    |
| ALP                    | 111    | < 73         | U/l    |
| γ-GT                   | 1      | < 5          | U/l    |
| AST (GOT)              | 85     | < 71         | U/l    |
| GLDH                   | 5      | < 11         | U/l    |
| Total protein          | 56     | 62 - 86      | g/l    |
| Albumin                | 34     | 29 - 46      | g/l    |
| Globulin               | 22     | 25 - 50      | g/l    |
| Albumin/globulin ratio | 1.5    | > 0.57       |        |
| Glucose                | 22.6   | 3.5 - 7.8    | mmol/l |
| Cholesterol            | 4      | < 8.5        | mmol/l |
| Fructosamine           | 325    | 190 - 365    | µmol/l |
| CK                     | 370    | < 542        | U/l    |
| LDH                    | 122    | < 182        | U/l    |
| Calcium                | 2.2    | 2.2 - 2.9    | mmol/l |
| Magnesium              | 0.7    | 0.6 - 1.1    | mmol/l |
| Total triglyceride     | 0.5    | 0.2 - 4.9    | mmol/l |

**Urine Tests:**

| Urine Tests        | Parameter                   | Finding   |
|--------------------|-----------------------------|-----------|
| Urine strip test   | Glucose                     | +++       |
|                    | Ketone                      | -         |
|                    | Protein                     | ++        |
| Refractometer      | USG                         | 1.024     |
| Clinical chemistry | UPC                         | < 0.4     |
| Microscopy         | Sediment                    | none      |
| Bacteriology       | Immersion medium (Uricult®) | No growth |

History, clinical picture, physical examination and laboratory results point to the presence of feline hyperthyroidism. With a total thyroxine (TT4) concentration that is elevated across the entire reference range, hyperthyroidism is the most important and indeed almost the sole differential diagnosis. Hyperthyroidism explains Remo's elevated liver values. It is known that around 90 per cent of all cats with hyperthyroidism exhibit moderately changed liver enzyme values. On a second glance, the fructosamine in the upper third of the reference range does not fit so well with the rest of the clinical picture. Internal medicine is the attempt to reconcile the clinical picture with the laboratory data. In the case of a genuine hyperthyroidism, an "almost pathogenic" fructosamine value around the 200  $\mu\text{mol/l}$  mark is to be expected. Fructosamines are non-enzymatically-catalyzed, saccharified serum proteins. The fructosamine concentration is thus mainly dependent on the serum glucose concentration and the concentration and half-life of the serum proteins. In everyday clinical practice, fructosamine is used in the diagnosis and monitoring of diabetes mellitus (DM). In the case of hyperthyroidism, the protein metabolism is increased and the half-life of the serum proteins reduced. In hyperthyroid cats, this results in the known phenomenon of low fructosamine concentration.

But let's return to our clinical case: The fructosamine is in the top third of the reference range and the serum glucose is significantly elevated at 22.6 mmol/l (407 mg/dl). The renal threshold for glucose has been exceeded and it shows up on the urine strip test: Glucose +++.

**In hyperthyroid cats, fructosamine is not suitable for the diagnosis or monitoring of diabetes mellitus.**

In a verified case of feline hyperthyroidism, due to the accelerated protein metabolism, fructosamine is not suitable for the diagnosis or monitoring of DM.

Remo was diagnosed via serial measurements of blood sugar with a portable measuring device (GlucoCalea® WellionVet). The monitoring was performed in the same way. Remo now receives one 2.5 mg Felimazole® tablet mornings and evenings and one unit of insulin glargine<sup>1</sup>, so that both disorders are well managed.

**Do polyendocrinopathies play a role in cats? What are the most common simultaneously occurring feline endocrine disorders?**

Polyendocrinopathies in cats play a fairly secondary role in everyday clinical practice. However, every veterinary practitioner specialising in pets is bound to encounter them in his/her professional life. There is only one study by two Canadian universities from 2010<sup>i</sup>, which prospectively collected information on 21 cases over 12 years. Six cats were excluded from the study, because e.g. the DM was iatrogenic. The most common combination in the study (in 10 out of 15 cases) was hyperthyroidism and DM. One half of the cats first succumbed to hyperthyroidism and the other half first succumbed to DM. Other reported combinations are hypercortisolism (hyperadrenocorticism, Cushing's disease) and DM, diabetes insipidus and DM, and finally hyperthyroidism and hyperparathyroidism. One weakness of the study is that the data was collected from university referral clinics. This means a considerable preselection of the patient population. Another weakness is the low number of included patients which means that the scope for statistical evaluation of the data is restricted. The low number of subjects with Cushing's disease and DM is surprising. The most specialised colleagues have probably encountered significantly more cases in a twelve year period. Even more surprising is that the clinically most frequent combination does not even merit a mention. According to literature and geography, behind one in five to one in ten cases of feline DM acromegaly is suspected.

## Is there a pathophysiological link between the various feline endocrinopathies apart from age?

The following table summarises the available information about the combinations:

| Combination of endocrinopathies | Interface between etiology and pathophysiology   | Clinical aspects   |
|---------------------------------|--|--|
| Hyperthyroidism/DM              | It is unlikely that hyperthyroidism and DM have a common underlying etiology. It is notable that hyperthyroidism results in reduced insulin sensitivity. For hyperthyroidism that is almost always the consequence of a functional adenomatous hyperplasia of both thyroid lobes, the etiology is multifactorial and not completely elucidated. Genetic, nutritional and environmental factors all seem to play contributory roles. Immune-related causes for the hyperthyroidism are not apparently involved. The etiopathogenesis of DM Type 2 is also multifactorial. Among possible factors that have been discussed are genetics, overweight, pancreatitis, amyloid deposits and much more. | One half of affected cats first succumbs to DM and the other to hyperthyroidism respectively. If hyperthyroidism is established, fructosamine is unsuitable for diagnosis and follow-up tests. If DM is present, total-T4 may be less sensitive in the diagnosis of hyperthyroidism.   |
| Acromegaly/DM                   | Acromegaly is a syndrome that is caused by excess growth hormone, which is created by a pituitary adenoma. The overproduction of growth hormone results, among other things, in insulin resistance, hyperglycemia and DM.  | Important differential diagnosis for non-adjustable DM. Probably one cat in ten is affected by DM. Diagnosis: Assay of IGF-I, which forms in the liver under influence of growth hormone. Important: Do not measure until four weeks after start of insulin therapy, in the case of acromegaly, it is only at this stage that an increase in IGF-I occurs. |
| Hypercortisolism/DM             | Hypercortisolism can be caused by a tumour of the hypophysis or of the adrenal cortex. Cortisol results in insulin resistance and hence in hyperglycemia.  | Nearly all cats with hypercortisolism have DM at the time of diagnosis.  |
| Hyperaldosteronism/DM           | No linkage to the pathophysiology reported to date.  | Both disorders can lead to a hypokalemia.  |

### <sup>1</sup>footnote on insulin glargine:

In Germany, the veterinary medicine *Caninsulin*<sup>®</sup> is licensed for the treatment of diabetes mellitus in cats, which is the medicine of choice depending on availability according to the cascade system.

### Reference

i Blois *et al* (2010) Multiple endocrine diseases in cats: 15 cases (1997-2008) *JFMS* 12(8):637-42

The treatments and doses described in this case study are entirely at the discretion of the author and are based on their own considerable clinical experience. It is the responsibility of individual prescribing veterinary surgeons to ensure that they comply with local veterinary medicine regulations.

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Dechra Veterinary Products Ltd, Sansaw Business Park, Hadnall, Shrewsbury, Shropshire, SY4 4AS

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