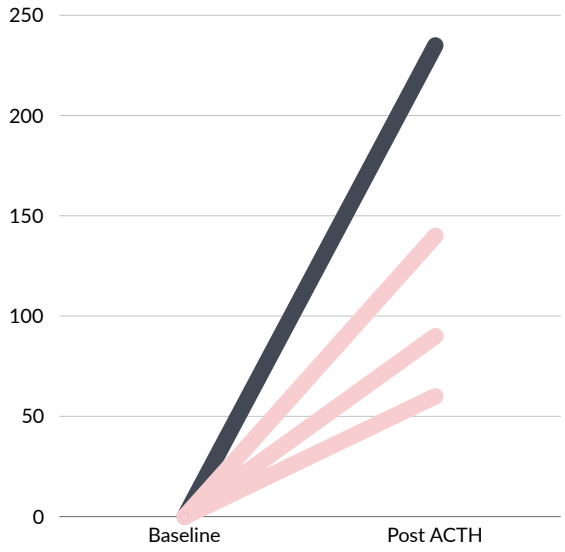
Canine Endocrinology

ACTH Stimulation Troubleshooting



First let's review the protocol: Cosacthen® (tetracosactide).

The official **dose** is, "0.25 mg (1 mL) per dog weighing 4.5–50 kg, administered by intravenous or intramuscular injection, with the purpose of performing the ACTH stimulation test."

Can a lower dose of Cosacthen® be used? Yes.
The Canadian label differs from the UK label. It is possible to use at the veterinarian's discretion an "off-label" dose of 5ug/kg as per the UK label.

Keep in mind that when using the 5 µg/kg dose, the maximal amount to be administered should not exceed 250 µg, even for dogs weighing more than 50 kg.

Test protocol: draw blood for a baseline cortisol, administer the ACTH, and then take blood one hour later for the post-ACTH cortisol measurement. There is no need to measure a 2 hour post-ACTH cortisol.

Make sure the tubes are labeled correctly as pre or post.

We are really small
Now what?

For dogs < 4.5 kg we have instructions as per Dechra's technical services:

"The safety study that was done for Cosacthen® (tetracosactide) was based on the maximum dose a dog in this weight range would receive, which is 250 µg (1ml) in a 4.5 kg dog (≈ 56 µg/kg). For this reason it cannot be recommended to give a dog weighing less than 4.5 kg the full vial of Cosacthen® (250 µg). Usage of tetracosactide at 5 ug/kg is effective and extra label dose is an alternative to the full vial."

Can you dilute it? NO!

"The issue is that 5 ug/kg in a 4.5kg dog corresponds to 0.09mL (Cosacthen®), which is very hard to measure accurately, and the product should NOT be diluted. As 0.1 ml (25 µg) is the minimum recommended volume to be drawn into a 1mL syringe, it makes sense for this to be the minimum dose/volume to be administered to dogs weighing 4.5 kg or less. "Since it is such a small volume, if you are worried that you may "lose" some product that remains in the needle and/or syringe hub, it should be safe to increase the total volume up to 0.2mL (50 ug). As an example, if you have a 2.5kg dog and you administer 0.2mL (50 µg), this corresponds to 20 µg/kg. We believe this should be safe, because this dose is still below the maximum dose of 56 µg/kg used in the safety study."

We have reviewed our ACTH product handling, protocol and the test procedure itself. Now what?

What drugs should be on my checklist?

One of my **favorite** proceedings is back from 2007 which is titled “Can I diagnose anything on glucocorticoids?” It is an oldie but a goodie. Oral steroids are an obvious source and will interfere with the cortisol assay if given on the same day but what about topical steroids?

Here are some drugs to consider which could significantly blunt an ACTH stimulation. The **“Allergy Shot” aka Triamcinolone IM ONCE** - the post ACTH cortisol is 50% suppressed at day 7 post administration and can take 22 days to return to normal. **Topical** steroids for skin or ears - especially **betamethasone, triamcinolone or fluocinonide** preparations can take effect within 7 hours and suppress the post ACTH cortisol within 5 days of repeated treatments. **Otic** administration of **dexamethasone or triamcinolone** BID in both ears caused a blunted ACTH stimulation within one week and a post ACTH cortisol range of 90-130 nmol/L. **Ocular** medication containing steroids, e.g., 4 weeks of topical **prednisolone** acetate in both eyes QID suppressed the post ACTH cortisol to approximately 40 nmol/L.

Herbal Supplements would be very rare but possible source of steroids.

Ketoconazole at high doses can potentially suppress an ACTH stimulation test.

Were you trying to rule out Addison's?

Is there an association between a blunted ACTH stimulation and inflammatory GI disease? Yes, but ...

this is NOT a means of diagnosing inflammatory GI disease. A blunted ACTH stimulation (post cortisol over 55 mol/L but below 221 nmol/L) could suggest further investigation for inflammatory bowel disease is warranted.

Is there a spectrum of disease? Could a blunted ACTH stimulation represent early Addison's disease?

Usually clinical signs are not expected until the post ACTH stimulation cortisol drops below 55 nmol/L. Could there be patients that do not adhere to this rule and could you catch a patient in the emerging phase of the disease? Yes it is possible and the likely reason why certain investigators and internists choose to use a post cortisol cut-off between 80 nmol/L to 121.4 nmol/L. Overall, we have seen cases that do represent a spectrum of disease but these are accurately documented and seen on rare occasion.

Addison's versus Cushing's

I expected an exaggerated response and I am certain my patient has not been exposed to exogenous steroids. Now what?

Dog's with adrenal based hyperadrenocorticism can on odd occasion have a blunted ACTH stimulation due to excess secretion of other hormones such as corticosterone or 17α-hydroxyprogesterone. Consider further investigation with ultrasound or advanced imaging in a dog that has clinical signs of HAC, a subnormal serum cortisol response on an ACTH stimulation test, and no history of exogenous glucocorticoid administration.

The very rare differentals for a blunted ACTH stimulation include:

Hemorrhagic infarcts, fungal infections or infiltrative adrenal gland disease secondary to lymphoma or metastatic disease would be obscure considerations that have been documented on rare occasion in veterinary and human medicine.

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