Monitoring the dog with Cushing's: is the ACTH stim dead?

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Since the introduction of trilostane for treatment of canine hyperadrenocorticism, an ACTH stimulation test conducted 3-5 hours post-pill has been recommended for use to guide treatment decisions. Two recent publications have cast serious doubt over this practice. The first one (Midense et al., JVIM, 2015) tried to solve the issue of there being no clear treatment guidelines for dogs with clinically well-regulated hyperadrenocorticism in which serum cortisol concentrations before and after an ACTH stimulation test are low (+/- < 50 nmol/l). Thirteen dogs with clinically well-regulated hyperadrenocorticism and pre- and post-serum cortisol concentrations <50 nmol/l 3-6 hours after trilostane administration were studied and had a second ACTH stim test performed 9-12 hours after trilostane administration, on the same day of the first ACTH stimulation test. What did they find? At this later point in the day the dogs showed plenty of ability to generate cortisol, i.e. had plenty of adrenal reserve. The investigators concluded that in dogs with clinically well-regulated, trilostane-treated, hyperadrenocorticism, though low cortisol concentrations before and after ACTH stim, trilostane treatment should not necessarily be stopped. Instead, the treatment could be continued, since the flatline ACTH stim did not predict a subsequent Addisonian crisis. Moreover, if these dogs had had their trilostane dose reduced, there clinical control would have worsened, affecting quality of life negatively. An extra safety valve might include screening for lack of stress leukogram or an ACTH stimulation test later on in the day. Nevertheless, in this particular study some dogs without lymphopenia still did not suffer an Addisonian crisis on follow-up.

The second recent study that puts the value of the ACTH-stim test in trilostane-treated hyperadrenocorticism dogs in doubt was published this year (MacFarlane et al., Vet Record, 2017) and compared the ability of various ways of cortisol measurement (including pre-pill serum cortisol, a 3-hours post-pill cortisol, as well as a traditional ACTH stimulation test) to discriminate between well-controlled and poorly-controlled dogs with hyperadrenocorticism. The result: all measures proved suboptimal, though the ACTH stimulation test performed the least well. The pre-pill cortisol actually outperformed all of them, leading to some endocrinologists to abandon the ACTH simulation test all together. As an alternative merely testing a morning serum cortisol, taken just prior to the trilostane, is being performed.

What should we do instead? As is the case in many endocrine patients, we need to focus on the clinical picture and use any additional endocrine tool as a guidance only, not as a mathematical tool. Until further evidence or superior tools become available, I would use the pre-trilostane serum cortisol in any clinically well-regulated trilostane-treated dog. If the clinical image suggests lack of control, we can increase the trilostane, or consider going BID, as long as this pre-cortisol is detectable. If the pre-trilostane cortisol becomes undetectable, the ACTH stimulation test might still be prudent, though we should also be paying attention to other tell-tell signs for oversuppression of the adrenals (including electrolyte changes and a lack of a stress leukogram). If a dog is unwell, we would err on the side of safety and perform an ACTH stimulation test regardless; a flatline response should be regarded as possible overdosing and treatment should be stopped.