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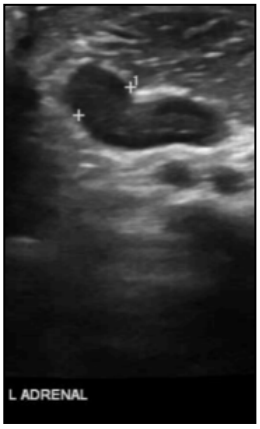
The Elusive and Misunderstood Adrenal Gland of the Canine Patient

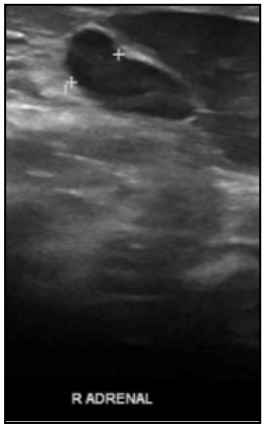
by Stacy Randall, DVM, DACVIM

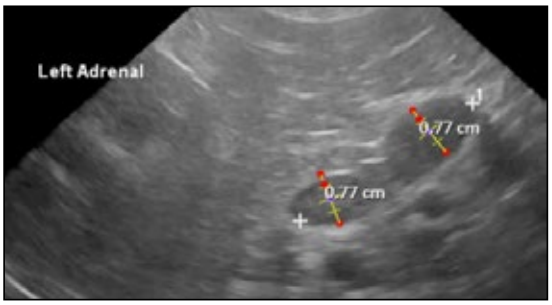
- *One of the most frustrating diagnoses to make is about the adrenal glands and specifically Hyperadrenocorticism. In school, we were given poster child cases of what a Cushing's dog looked like; how to test and what the results should be, and how to treat. Most of our patients do not read these textbooks and are not that easy to identify, diagnose and treat.*

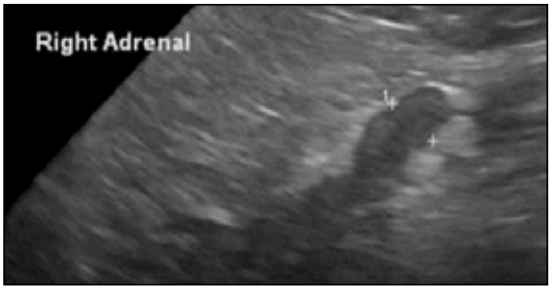
- *Here is just an overview of my takeaway points on the adrenal gland and diagnosing Hyperadrenocorticism in the dog. Of course, there are many different thoughts and variable discussions on the best test, how to correctly interpret the tests, etc. – this is just my take over 30 years and what I have found to serve me well.*

LET'S START WITH ULTRASOUND









First you have to find it! Here are some pointers for locating the elusive adrenal gland on ultrasound.

Left Landmark:
The celiac and cranial mesenteric arteries are cranial and the left renal artery is caudal. The left phrenicoabdominal vein is the dorsal landmark. Often, one can identify the "hook" which is the renal artery coming alongside and over the adrenal.

Right Landmark:
Nestled up along the right phrenicoabdominal vein and caudal vena cava, which is ventral and lateral.

Normal size:
The caudal pole of the adrenal gland is the consistent region to measure and has been demonstrated to be a reliable indicator. The measurement of the thickness in the saggital plane is recommended. The use of the cranial pole measurement has

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not been verified to be reliable and is variable. The measurement of both poles is beneficial when trying to determine variable pole enlargement as with a possible functional tumor or atrophy.

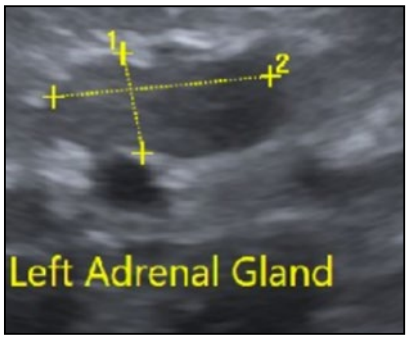
Adrenal length is not consistently correlated and should not be used to determine adrenal disease. The caudal pole does have a variation between <0.55 cm; <0.65 cm; and <0.75 cm for a 10, 20 or 40 kg dog respectively. The canine left adrenal gland can have variable shapes described as a peanut or bean, lawn chair, flattened or bi-concave, and are all variations of normal. The right is more likely to be oval or pancake in appearance.

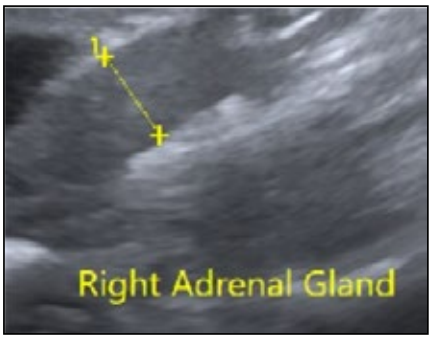
DISEASES OF THE ADRENAL GLAND

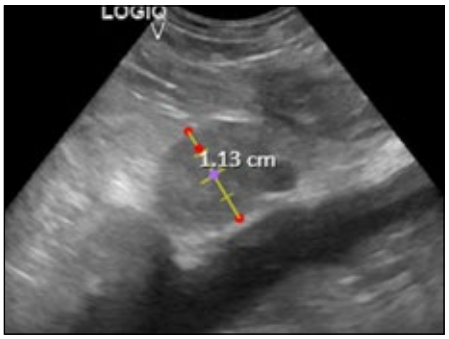
1. Hyperadrenocorticism – a cortical disease of the zona fasciculata
2. Hypoadrenocorticism – a cortical disease of the zona glomerulosa
3. Pheochromocytoma – medullary related to epinephrine and norepinephrine
4. Adrenal Hyperplasia-like syndrome -mimics Cushing's but is a congenital imbalance of either growth or sex hormones. Poms, Samoyeds, Chows, Toy Poodles, and Keeshond's
5. Neoplasia

ADRENAL DISEASES ON ULTRASOUND

1. Hyperadrenocorticism:
Bilaterally prominent, enlarged, rounded, and nodular but can be asymmetric with PDH. An adrenal tumor will be large or prominent, and sometimes have mineralization or a defined nodule but the hallmark is contralateral atrophy. As it is an adrenal tumor that is secreting the cortisol and the pituitary is normal, there will have been shut down of the slow and fast feedback controls and the normal adrenal is not functioning and is small due to disuse.







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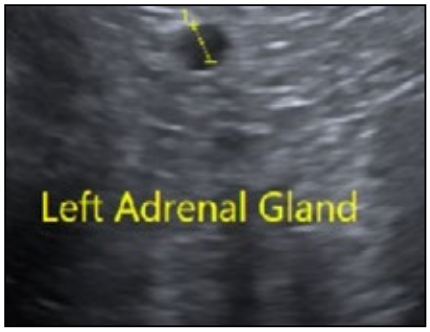
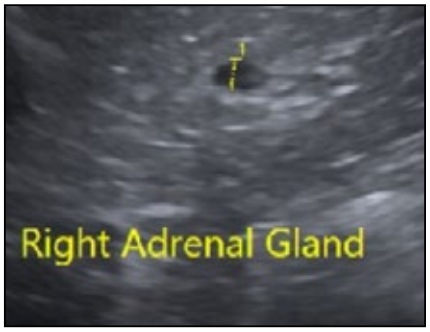
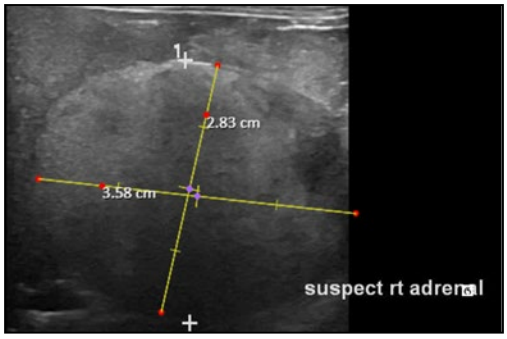
2. Hypoadrenocorticism:
Should be small, flat, or even not visualized. Early in the disease, they can be normal to even prominent before atrophy – size does not rule out insufficiency. If you are seeing small adrenal glands, especially in the ill patient, usually suggests disuse atrophy from exogenous steroids or concern for Hypoadrenocorticism. Remember that Addison's is the great imitator and can look like anything and have very vague signs.





3. Pheochromocytoma:
Often a large, mass effect, sometimes invading and possibly mineralized. The other pole on the affected side and the contralateral adrenal gland can be normal or even prominent from stress and illness. The blood pressure is the first tip-off along with the episodic behavior often mentioned.



4. Adrenal Hyperplasia-like syndrome:
Prominent and similar to PDH or normal.

5. Neoplasia:
Rounded, large, nodular, invasive, or mineralization noted.

TESTING FOR ADRENAL DISEASES

Here lies the controversy. So, to understand the testing, we need to go back and remember freshman endocrine pathophysiology and the Hypothalamic-Pituitary-Adrenal Axis (HPA). Simply, the HPA regulates the formation and control of the steroids in the body. This is the basis of the endocrine testing that we perform to diagnose adrenal issues in our companions.

a. Urine cortisol: creatinine ratio

The idea is that dogs with Cushing's should have higher circulating cortisol in the blood and hence should then have higher urine cortisol when quantitated with creatinine. With this in mind, then the question is whether there will be a lower UCC with hypoadrenocorticism. Overall, a normal UCC is a relatively good and easy way to rule out presumptive Cushing's; however, cannot be confirmed as a diagnosis if elevated as it can be elevated for several conditions and non-adrenal gland diseases where stress is involved.

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b. ACTH stimulation

Originally, the ACTH stimulation test had 3 uses. To screen for possible Hyperadrenocorticism, diagnose Hypoadrenocorticism, and for monitoring therapy of Cushing's patients. It has a lower sensitivity but higher specificity for Hyperadrenocorticism than the LDDST. It is better at ruling out the disease if not present and can be superior if there is a significant non-adrenal illness. That being said, it can also be severely exaggerated in cases making Cushing's appear the likely problem when, in fact, it is not. To use an ACTH stimulation or a Low-dose dexamethasone suppression test is the area of much controversy and variable thoughts on the "test of choice". It depends on how you were taught and your experience and confidence levels.

c. Low-dose dexamethasone suppression test

If a normal dog, even if stressed in the hospital environment, is administered exogenous steroids, there should be a negative feedback control at both the fast and slow feedback pathways that shut down the formation of endogenous steroids. This happens usually by 3-4 hours and should be switched off for 8 hours or more. In a perfect world, the patient will suppress to the lowest point by 4 hours and maintain at that level without variation for at least 8 hours. If appropriate suppression and no variation, not Cushing's. The problem with this interpretation is in the cut-off levels for the laboratories and when there are variations. Most labs have a <1.4 cut-off for normal suppression. In my opinion, that is way too high – most normal dogs will suppress to less than <0.5 and often down at <0.2 by 4 hours. Also, there is controversy on what it means if there is variation between the 4 and 8-hour samples. For me, the normal dog will suppress to <0.5 by 4 hours and maintain at that exact level for at least 8 hours without any variation. Any progressive suppression or suppression and escape even still in the normal range would suggest early loss of feedback control and Pituitary Dependent disease. Adrenal tumors are basically a wildfire and do what they want and rarely will vary or suppress with low-dose steroid administration.

d. High-dose dexamethasone suppression test

The High dose dexamethasone suppression test is the same idea with a higher level of exogenous steroid administration with the thought that some Cushing's dogs will not suppress at low levels but will at higher levels and should be the discriminating test to discern a pituitary disease from adrenal disease. With the advent of ultrasound and visualization of the adrenal glands, it is almost always now a moot point as the ultrasound will give the information needed and avoid the need for a HDDST. I don't think I have performed one in 15 years or more.

e. Endogenous ACTH

Endogenous ACTH measures the circulating level of ACTH in the blood. The problems are the availability of the test; the special handling required and that you actually need to do the push-ups above and can't just use an endogenous ACTH test and have your answer. Again, with the advent of ultrasound and visualization of the adrenal glands routinely, usually not a necessary test anymore. It is accurate but timely in turnaround, cost, availability, and special handling. In essence, based on the HPA, a Pituitary dependent dog will have normal or elevated levels of ACTH as the disease is arising from excess CRH or ACTH in the pituitary while an adrenal tumor dog has the secretion of excess steroids in the adrenal tumor and the feedback works fine and the pituitary is shut down. Unfortunately, as there can be variations in the levels, even if readily available and cost-effective, would be difficult to interpret in most cases as a sole test modality.

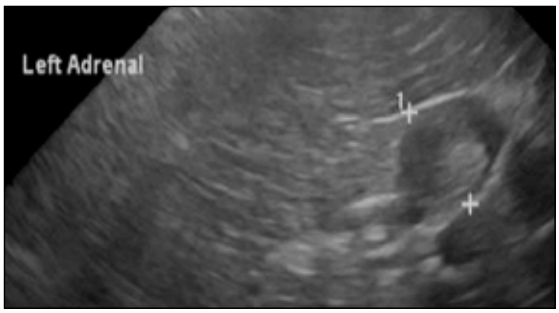
CASE PRESENTATION

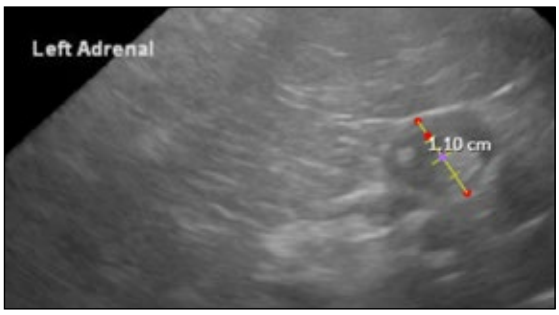
Signalment: 12-year, 6-month-old F/S mixed breed canine.

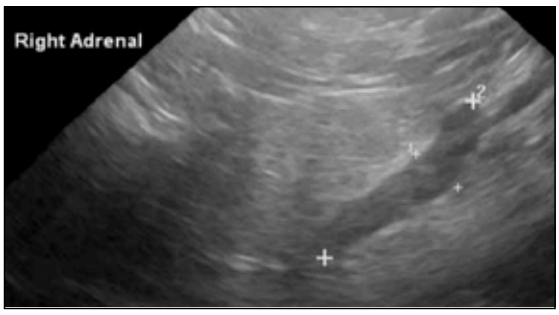
History: The patient originally presented one year ago with a history of proteinuria. No clinical signs were suggestive of Cushing's. There was an increased UPC, normal Blood pressure at 150 mmHg, and an elevated ALP of 786. The left adrenal gland was not clearly defined while the right was prominent measuring 0.75 cm in the cranial pole and 0.69 cm in the caudal pole. A low dose dexamethasone suppression test was abnormal LDDST - Pre - 2.9; 4 hour - 1.1; 8 hour - 1.7. This demonstrated some suppression and escape. As the patient was asymptomatic, the proteinuria was monitored and treated.

Progression: A year later, the patient represents with ataxia and petite mal seizures or possibly small TIAs. There has been some progression in the ALP at 911 while the UPC is 1.9. Recheck ultrasound demonstrates bilateral but asymmetric adrenomegaly with the right adrenal gland mildly more pronounced than previously imaged measuring 0.8 cm while the cranial pole has a rounded and hyperechoic region measuring up to 0.87 cm. The left adrenal gland has a rounded, and coarse cranial pole measuring 0.72 cm and the caudal pole 1-1.2 Cm. There is a rounded and hyperechoic nodule measuring 0.7 by 0.57 cm in the caudal pole. There is a second small hyperechoic nodule also noted. LDDST - pre 3.5 (1-5) 4 hr 1.0 (0-1.4) 8hr 2.0 (0-1.4) .

Plan: Now with clinical signs, concern for possible thromboembolic disease, and the progressive changes both in the LDDST and the appearance, treatment will begin.







TAKE HOME POINTS

1. Adrenal gland disease can be frustrating for you and your client. Have the owner prepared that there may be several tests and some frustration – manage expectations.
2. Even if the owner does not think the patient has polydipsia if you think otherwise, have them quantitate the water consumption – often it is slowly progressive for months and they have become used to it and don't recognize it.
3. Ask if they are using any topicals, "salves", dermatologic, otic or ophthalmologic – many owners are not aware of how common topical steroids are.
4. Always take a blood pressure.
5. Adrenal ultrasound can be frustrating no matter how good an ultrasonographer you are – some dogs image ugly and with gas distraction, panting, hepatomegaly, etc sometimes it is difficult to catch the adrenal glands
6. When thinking Cushing's and you have done the testing – don't put normal in the history, please submit the values so the reader can look for subtle changes that may have been interpreted as normal yet aren't.
7. If you diagnose PDH, always start the Trilostane at a low dose divided bid dosing:
    a. If you start sid and want to increase to bid – some owners will balk.
    b. If there are still clinical signs but the post-treatment ACTH is "normal", the trilostane may only be working 12 hours and not 24, and hence the continued signs.
    c. Some dogs can be monitored if doing well with pre-trilostane cortisol and not an entire ACTH stimulation. Others, can't and need the full ACTH.
    d. If you have questions, reach out…

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Stacy R Randall graduated from the University of Florida in 1990. After 2 years in private practice in Florida, she completed a 3 year internal medicine residency at Purdue University with special emphasis on renal, endocrine, ultrasound and oncology. She settled back in Florida and started the Internal Medicine service at Affiliated Veterinary Specialists in 1996 and was there until 2004.

Stacy began consulting in teleradiology in 2003. A move to San Antonio, TX in 2004 occurred to start an Internal Medicine Service at South Texas Veterinary Specialists and she was there until 2013. Stacy transitioned to a full time Antech position in 2011.