Fig. 18.1. Regulation of cortisol and aldosterone secretion.

- CRH released from the hypothalamus stimulates the production and release of ACTH from the pituitary gland. ACTH stimulates the production and release of cortisol and aldosterone from the adrenal gland cortices. In the negative-feedback system (dashed lines), increasing the [cortisol] inhibits the secretion of CRH and ACTH.
- Increased [angiotensin II], hyperkalemia, hyponatremia, and increased [ACTH] promote the release of aldosterone from adrenal gland cortices. Atrial natriuretic peptide inhibits aldosterone release. The secreted aldosterone stimulates the renal retention of Na^+ and Cl^- and excretion of K^+ and H^+.

Fig. 18.2. $(Cort : Crt)_u$ ratios in two studies.

- In study A, the $(Cort : Crt)_u$ ratios from three groups of dogs were compared to a group of healthy dogs (background grey region; mean = 13×10^{-6}, n = 31). Of 25 dogs with hyperadrenocorticism (21 PDH and 4 FAN), 23 had increased $(Cort : Crt)_u$ ratios. Of 21 dogs with nonadrenal disorders (renal insufficiency, liver disease, pyelonephritis, hypothyroidism, bronchitis, and diabetes insipidus) but in which hyperadrenocorticism was suspected, only one had an increased $(Cort : Crt)_u$ ratio. However in 28 dogs with moderate to severe nonadrenal disorders (gastrointestinal, renal, lower urinary tract, liver, neurologic, immune-mediated, cardiac, traumatic, and infectious diseases), 22 had increased $(Cort : Crt)_u$ ratios.[26]
- In study B, the $(Cort : Crt)_u$ ratios from dogs with hyperadrenocorticism (36 with PDH and 4 with FAN) and other polyuria/polydipsia disorders (diabetes insipidus, hypercalcemic disorders, liver disease, pyometra, and diabetes mellitus) were compared to the $(Cort : Crt)_u$ ratios found in healthy dogs (background grey region; mean = 6×10^{-6}, n = 20). All 40 dogs with hyperadrenocorticism had an increased $(Cort : Crt)_u$ ratio but so did 18 of the 23 polyuria/polydipsia (PU/PD) dogs that did not have hyperadrenocorticism.[27]

Fig. 18.3. ACTH concentrations in adrenocortical disorders of dogs and cats.

- Dogs with PDH and primary hypoadrenocorticism have ACTH concentrations WRI or increased, whereas dogs with FAN and secondary hypoadrenocorticism have ACTH concentrations below reference intervals. The background grey region represents the canine reference interval. Data for the graph were extracted from published concentrations.[30,66]
- Cats with PDH and primary hypoadrenocorticism have increased ACTH concentrations, whereas cats with FAN have decreased ACTH concentrations. The background grey region represents the feline reference interval. Data for the graph were extracted from published concentrations.[66]

Note: The arrows above the solid bars indicate that concentrations may be much greater than the values shown in the *y*-axes.

Fig. 18.4. Responses for canine dexamethasone suppression tests.

- Data for A and F are results expected for healthy dogs, based on common decision limits. Suppression was defined as a postdexamethasone [cortisol] < 1.4 μg/dL and < 50 % of predexamethasone concentration.
- Data for B–D, G, and H were extracted from published results.[67] In B and D, suppression was defined as a postdexamethasone [cortisol] < 1.4 μg/dL. In C, suppression was defined as a postdexamethasone [cortisol] < 50 % of the predexamethasone concentration. In G and H, suppression was defined as a postdexamethasone [cortisol] < 1.4 μg/dL or < 50 % of the predexamethasone [cortisol].
- Data for E were extracted from published results;[68] comparative data for HDDST (I) were not found. In the LDDST, suppression was defined as a postdexamethasone [cortisol] < 30 nmol/L (1.1 μg/dL), a decision limit estimated from graphical data. Nonadrenal disorders included hepatic, pancreatic, urinary, gastrointestinal, respiratory, and cardiac diseases and endocrine disorders other than hyperadrenocorticism (e.g., diabetes mellitus, hyperparathyroidism, and insulinoma). Dogs selected for this group were not suspected of having hyperadrenocorticism.
- Using the LDDST, all dogs with FAN (D), most dogs with PDH (B and C), and many dogs with nonadrenal illnesses (E) had inadequate suppression. Using a < 50 % criterion for suppression (C), more dogs with PDH had adequate cortisol suppression than when judged by the < 1.4 μg/dL criterion (B). Using the < 1.4 μg/dL criterion, 48 of 51 (94 %) PDH dogs that had suppression at 4 h had escaped suppression by 8 h. Using the < 50 % criterion, 58 of 102 (57 %) PDH dogs that had suppression at 4 h had escaped suppression by 8 h.
- Using HDDST, nearly all dogs with FAN (H), but a minority of dogs with PDH (G), failed to have adequate suppression at the 4 h and 8 h samplings.
- If results from LDDST and HDDST are examined together,[67] there was inadequate suppression of cortisol concentrations in both tests in nearly all dogs with FAN (D and H; 94 %) but in a minority of dogs with PDH (B, C, and G; 24 %). A few dogs with PDH (14 %) and two dogs with FAN (6 %) had inadequate suppression with the LDDST but had adequate suppression with the HDDST. Two dogs with PDH (1 %) had adequate suppression with the LDDST but inadequate suppression with the HDDST.

HD, high dose; and LD, low dose.

Fig. 18.5. Responses from canine ACTH stimulation tests.

- Criteria used to determine appropriate, inadequate, or exaggerated responses to ACTH stimulation varied among publications. For each set of extracted data, the authors' criteria were used.
- In all hypoadrenocorticism cases, there were inadequate responses to ACTH stimulation. The 225 cases included 220 cases of primary idiopathic hypoadrenocorticism and five cases of secondary hypoadrenocorticism.[69]
- In all cases of iatrogenic hyperadrenocorticism, adrenocortical atrophy resulted in inadequate responses to ACTH stimulation.[70]
- In 84 % of PDH cases and in 51 % of FAN cases, there were exaggerated responses to ACTH stimulation.[35,60,68,71–74]
- In 14 % of dogs with nonadrenal illnesses, there were exaggerated responses to ACTH stimulation.[68]