Recent Advances in the Diagnosis of Cushing's Syndrome in Dogs

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KEYWORDS

- Hypercortisolism • Pituitary-adrenocortical axis
- Urinary corticoids • Adrenocorticotropic hormone
- Diagnostic imaging

Hypercortisolism is a common condition in dogs and can be defined as the physical and biochemical changes that result from prolonged exposure to inappropriately high plasma concentrations of (free) cortisol, whatever its' cause. This disorder is often called Cushing's syndrome, after Harvey Cushing, the neurosurgeon who first described the human syndrome in 1932.

Cushing's syndrome is sometimes iatrogenic, in most cases due to administration of glucocorticoids for the treatment of a variety of allergic, autoimmune, inflammatory, or neoplastic diseases. The development of clinical signs of glucocorticoid excess depends on the severity and duration of the exposure. The effects also vary among animals owing to interindividual differences in cortisol sensitivity. Corticosteroid administration causes prompt and sustained suppression of the hypothalamic-pituitary-adrenocortical axis. Depending on the dose and the intrinsic glucocorticoid activity of the corticosteroid, the schedule and duration of its administration, and the preparation or formulation, this suppression may exist for weeks or months after cessation of the corticosteroid administration.

This article focuses on the diagnosis of spontaneous hypercortisolism. In 80% to 85% of the spontaneous cases, hypercortisolism is adrenocorticotropic hormone (ACTH)-dependent, usually arising from hypersecretion of ACTH by a pituitary corticotroph adenoma. Ectopic ACTH-secretion syndrome is rare in dogs.[1] The remaining 15% to 20% of cases of spontaneous hypercortisolism are ACTH-independent and result from autonomous hypersecretion of glucocorticoids by an adrenocortical adenoma or adenocarcinoma. In addition to an adrenocortical tumor, ACTH-independent hypercortisolism can be caused by bilateral (macro)nodular adrenocortical

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hyperplasia because of aberrant adrenal expression of either ectopic or overactive eutopic hormone receptors.[2–4]

CLINICAL MANIFESTATIONS OF HYPERCORTISOLISM

All endocrine tests used for the diagnosis of endogenous hypercortisolism entail measurement of cortisol in plasma or urine (or saliva). Regardless of which test is used, a high degree of clinical suspicion is mandatory to avoid false-positive test results. Positive test results in patients that have developed several clinical signs of Cushing's syndrome over a relatively short period of time are more likely to be diagnostic than positive test results obtained in patients with more unusual presentations. Obviously, presentations that are more unusual require more confirmatory tests than a dog with a typical history and clear-cut physical and biochemical changes. Notably, several dogs with Cushing's syndrome do not present the full-blown picture originally described in textbooks. Instead, they often have milder hypercortisolism with less pronounced symptomatology. Thus, making a diagnosis requires considerable clinical insight.

Spontaneous hypercortisolism is a disease of middle-aged and older dogs, although, very rarely, it may occur as early as 1 year of age. There is no gender predilection. It occurs in all dog breeds, with a slight predilection for small breeds such as dachshunds and miniature poodles. The incidence is much higher in dogs than in humans and cats and has been reported to be 1 to 2 cases per 1000 dogs per year.[5]

Many of the clinical signs can be related to the biochemical effects of glucocorticoids, namely increased gluconeogenesis and lipogenesis at the expense of protein (**Fig. 1**). In dogs, the cardinal physical features are centripetal obesity and atrophy of muscles and skin (**Fig. 2**). Polyuria and polyphagia are also dominating features. The polyuria is known to be due to impaired osmoregulation of vasopressin release and interference of the glucocorticoid excess with the action of vasopressin in the

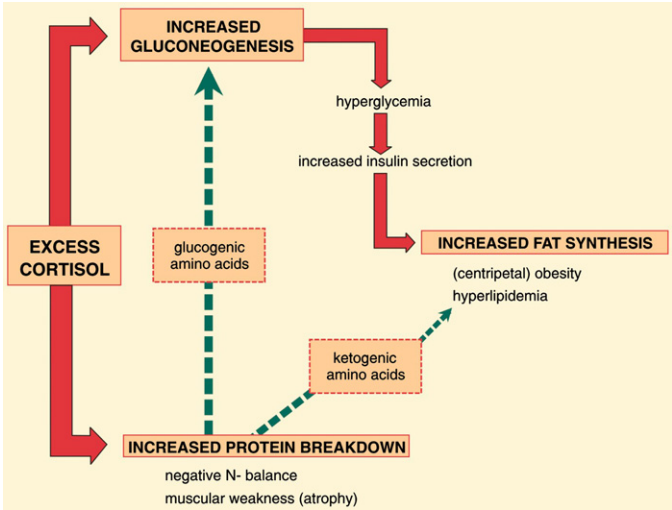

Fig. 1. Effects of cortisol excess. Increased gluconeogenesis leads to hyperglycemia, which is controlled initially by increased insulin secretion. This causes increased lipogenesis. Thus, the result of glucocorticoid excess is the catabolism of peripheral tissues such as muscle and skin to deliver the substrate for increased gluconeogenesis and lipogenesis.