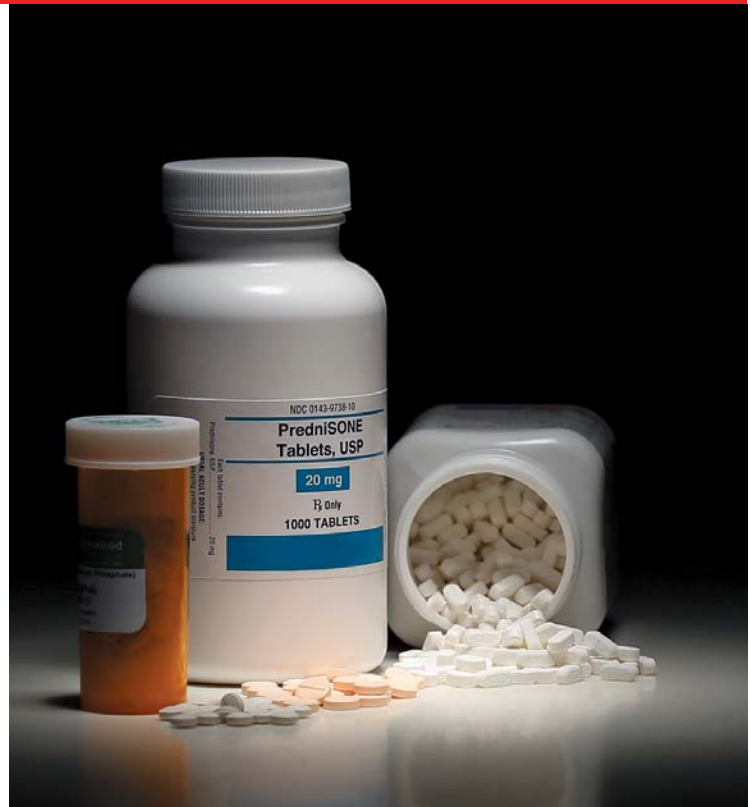


Glucocorticoids

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Glucocorticoids (GCs) have far-reaching pharmacologic effects¹ that can vary considerably with the dosage and vary somewhat with the type of GC prescribed (see **Far-Reaching Pharmacologic Effects of Glucocorticoids**).

Prednisone, Prednisolone, and Methylprednisolone

Prednisone is a prodrug of the active drug prednisolone.² In cats, oral prednisolone results in much higher plasma prednisolone concentrations than the same dose of oral prednisone, with a 4-fold higher area under the curve.³ This may be because of the low bioavailability of prednisone in cats or a sluggish conversion to prednisolone. For this reason, prednisolone is the preferred GC in cats. In contrast, dogs can readily interconvert prednisone and prednisolone.²

Methylprednisolone is more potent than

prednisolone at inhibiting in vitro lymphocyte proliferation in humans.^{3,4} Similar data are not available for dogs. Methylprednisolone is reported in companion animal textbooks to have no mineralocorticoid effects when compared with prednisolone,⁵ but the evidence for this is difficult to find. In fact, methylprednisolone does activate mineralocorticoid responsive renal pathways, at least in rodents.⁶

Dosing of Prednisone, Prednisolone, and Methylprednisolone

Commonly used GC dosages were extrapolated from older human studies and supported by clinical experience in dogs and cats (see **Empirical Recommendations for Glucocorticoid Dosing**). For physiologic replacement, the recommended starting dosage is 0.2 mg/kg PO once a day. Timing appears to be unimportant, at least in cats.⁷

FAR-REACHING PHARMACOLOGIC EFFECTS OF GLUCOCORTICIDS¹

- ▶ Decreased inflammatory mediator production
- ▶ Impaired leukocyte phagocytosis, chemotaxis, and antigen processing
- ▶ Pronounced catabolic effects on metabolism, muscle mass, and bone turnover
- ▶ Altered renal calcium, sodium, and potassium excretion
- ▶ Initiation of a stress leukogram
- ▶ Induction of serum alkaline phosphatase

Dosages that are approximately 3-fold higher have been recommended for stress (eg, hospitalization or surgery) in animals that have endogenous GC deficiencies.^{8,9} This is supported by studies of cortisol secretion in dogs under experimental stress conditions.^{8,9}

For anti-inflammatory effects, oral dosages of 0.5 to 1.0 mg/kg per day for dogs and 1.0 to 2.0 mg/kg per day in cats are recommended; for immunosuppression, 2.0 mg/kg per day or 50 mg/m² in dogs or up to 4.0 mg/kg per day in cats is suggested.

For large- and giant-breed dogs, the use of no more than 50 mg/m² (maximum dosage of 30 to 40 mg twice per day) is suggested by the author to decrease the incidence of severe adverse effects (eg, muscle wasting, secondary infections). In overweight cats, the dosage of prednisolone should likely be based on estimated lean body weight, as plasma prednisolone concentrations are approximately 2-fold higher in obese cats when compared with normal-weight cats given the same dosage/kg.³

Prednisone, prednisolone, and methylprednisolone all have some mineralocorticoid effects,⁶ and moderate-to-high dosages should be avoided in patients with hypertension, heart failure, ascites, or hypokalemia. Further, methylprednisolone acetate can lead to acute plasma volume expansion and even congestive heart failure in cats, although this has been attributed to intercellular fluid shifts rather than overall water retention.^{10,11}

GCs typically induce serum alkaline phosphatase (ALP) activity in dogs, with lesser increases in alanine aminotransferase (ALT). These changes are not clinically actionable on their own unless ALT activity approaches or exceeds ALP or if hyperbilirubinemia is present, each of which suggests a different disease process.

In contrast, ALP does not appear to be readily induced by GCs in cats⁷; small increases in ALP compared to baseline have been reported in cats given methylprednisolone acetate, but no values were outside of range.⁸ Any increase in serum ALP outside of the reference range is clinically important in cats, regardless of whether they are being treated with GCs.

Anti-inflammatory prednisone dosing suppresses the hypothalamic-pituitary-adrenal (HPA) axis by week 2 of treatment.¹² After 1 month of treatment, adrenal function can take another 2 weeks to recover.¹² Because of this, patients should ideally be weaned off chronic GCs at least 2 to 3 weeks before elective anesthesia or surgery if possible; however, the potential negative implications of stopping treatment should be considered for each patient.

Dexamethasone

Dexamethasone is approximately 5 to 10 times more potent than prednisone,⁹ with a duration of action of approximately 32 to 48

Prednisolone is the preferred glucocorticoid in cats.

Disadvantages and Adverse Effects

Glucocorticoids commonly cause dose-dependent polyuria and polydipsia, muscle wasting, and alopecia in dogs. Cats appear to be more resistant to many GC adverse effects, possibly due to fewer and lower-affinity GC receptors in the liver and skin.⁵ Acquired diabetes mellitus is the major complication of chronic GC treatment in cats, and it requires careful clinical monitoring for polydipsia, weight loss, or glycosuria.

hours. Dexamethasone has no mineralocorticoid activity due to a methyl ring substitution⁶ and should not promote salt and water retention.

Indications and Dosing

Dexamethasone is likely to be the preferred GC in patients with preexisting hypertension, heart failure, hypoalbuminemia, edema, or ascites. Based on dexamethasone's increased potency,⁹ dosages can be determined empirically by calculating the target prednisone dose and dividing by 7 or 8 to get an equivalent dexamethasone dose. Dexamethasone is also available in an injectable form, which is useful for SC administration to bypass severe malabsorption when treating protein-losing enteropathy or lymphangiectasia.

Disadvantages and Adverse Effects

Dexamethasone (0.55 mg/kg PO per day) is more diabetogenic in healthy cats than prednisolone at 8 times the dosage (4.4 mg/kg PO per day).¹⁰ This suggests that dexamethasone is at least 8 times as potent as prednisolone in cats.

Dexamethasone is not appropriate for alternate-day therapy due to its long duration of action. During chronic tapering courses, dexamethasone can be switched to prednisone or prednisolone when lower doses are reached (eg, equivalent to 0.5 to 1.0 mg/kg PO of prednisone per day) and alternate-day treatment is indicated.

Budesonide

Budesonide is an orally administered GC with high first pass clearance in humans.¹¹ In dogs, budesonide is less likely to increase liver enzymes or cause a stress leukogram. It also may cause less PU/PD in some dogs.^{12,13}

Indications and Dosing

Budesonide offers an alternative to prednisone or prednisolone for the treatment of

In dogs, budesonide is less likely to increase liver enzymes or cause a stress leukogram.

inflammatory bowel disease¹⁴ and possibly inflammatory liver diseases. It appears to have concentrated local effects; this makes it an attractive alternative therapy for inflammatory bowel disease, with equivalent efficacy when compared with prednisone in dogs.¹³

Although the published empiric dosage is 3 mg/m² once a day,¹² this dose can still cause marked PU/PD and panting in some dogs and can completely suppress the HPA axis.^{12,13} Lower starting dosages (eg, 1-2 mg/m² or 1-2 mg/30 kg [dogs]; 0.5-0.75 mg [cats]) may be better-tolerated and can be titrated to clinical effect.

Triamcinolone

The reported potency of triamcinolone relative to prednisolone has a wide variability, from 10:1 to 1:1; however, in a study of cats with pruritic skin disease, triamcinolone at one-seventh the dose (0.18 mg/kg/day PO) showed comparable efficacy to methylprednisolone (1.41 mg/kg/day PO), suggesting that triamcinolone may be 7 times more potent than methylprednisolone in cats.¹⁵ This study also found a lower incidence of PD in cats treated with triamcinolone when compared with methylprednisolone, although the number of cats in the study was small.¹⁵ This finding is consistent with the understanding that triamcinolone, like dexamethasone, has a ring substitution that ablates mineralocorticoid activity.⁶

The potency or efficacy of oral triamcinolone has not been compared directly to

PU = polyuria
PD = polydipsia

TABLE

EMPIRICAL RECOMMENDATIONS FOR GLUCOCORTICOID DOSING

Indication	Dogs (prednisone or prednisolone)	Cats (prednisolone)
Physiologic replacement	0.2 mg/kg/day PO (2–3 fold increases for stress)	0.2 mg/kg/day PO (2–3 fold increases for stress)
Anti-inflammatory	0.5–1.0 mg/kg/day PO	1.0–2.0 mg/kg/day PO
Immunosuppression	2.0 mg/kg/day (no higher than 50 mg/m ²)* PO	2.0–4.0 mg/kg/day PO

*Dosing on m² basis is recommended anecdotally in large dogs to avoid debilitating adverse effects.

dexamethasone or prednisone in dogs. Triamcinolone is more commonly used in its long acting injectable formulation (Vetalog, bi-vetmedica.com) in dogs.

Long-Acting Injectables

Longer-acting injectable GCs provide sustained release by slow dissolution of acetonide and acetate formulations. These GCs offer convenience for difficult-to-pill patients, but prolonged use can lead to suppression of the HPA axis and functional adrenal insufficiency in times of stress. For example, triamcinolone acetonide (Vetalog, bi-vetmedica.com) lasts weeks, and a single injection can suppress adrenal function for up to 4 weeks in dogs.¹⁶

Like oral GCs, these injectable GCs can cause debilitating adverse effects, which are more difficult to reverse because of prolonged duration of action.

Both triamcinolone acetonide and methylprednisolone acetate (DepoMedrol, henryschein.com) can precipitate congestive heart failure in susceptible cats.¹⁷ This is attributable to an increase in plasma volume of up to 40% in cats within the first week after GC administration.¹⁸ This appears to be secondary to osmotic shifts between the cellular and plasma compartments.¹⁸

These long-acting GCs should be avoided in patients with a history of heart failure and should be used only with client education and careful clinical monitoring in patients with cardiac murmurs.

Similarly, methylprednisolone acetate increases blood glucose levels in cats¹⁸ and can precipitate overt diabetes mellitus. Any cat treated with a GC—particularly those given intermittent long-acting injectables—should be monitored closely for new PD, weight loss, glycosuria, or rising serum fructosamine concentrations.

Like oral GCs, these injectable GCs can cause debilitating adverse effects, which are more difficult to reverse because of prolonged duration of action.

Bacteriuria without clinical signs develop in about 20% to 40% of dogs treated with GCs chronically; females appear to be at a higher risk than males.^{19,20} Bacteriuria can be seen even with alternate-day therapy, and monitoring urine sediment alone is unreliable because half of positive cultures lack pyuria

in GC-treated dogs. However, current evidence in humans does not support the treatment of asymptomatic bacteriuria, even in immunocompromised patients.^{14,15} Therefore, periodic urine cultures are probably not indicated in dogs and cats treated with GCs, unless urinary signs are noted. ■

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