

Peer Reviewed

Inhaled Corticosteroids & Airway Disease

You have asked...
Are inhaled corticosteroids effective for managing chronic inflammatory airway disease?

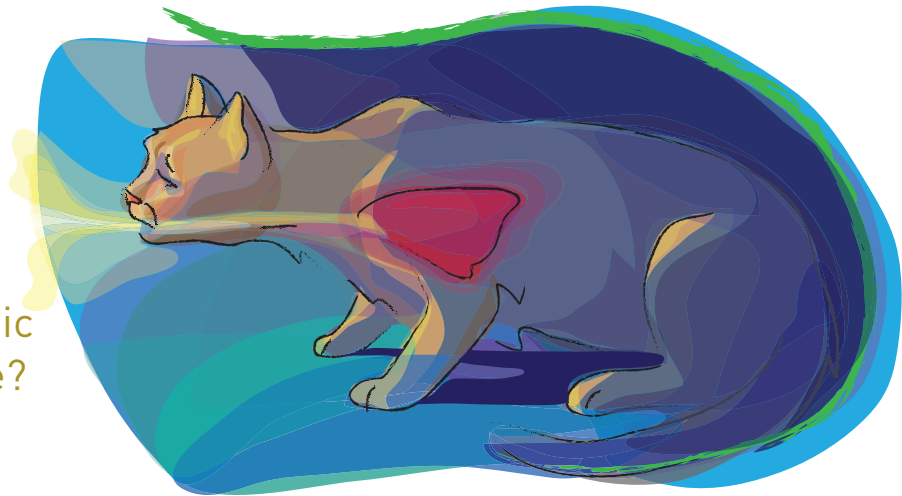


Illustration by Bill Celandier

The expert says...

Airway disease is classified as acute or chronic. Acute airway disease is represented by such conditions as infectious tracheobronchitis, while common chronic airway diseases include canine chronic bronchitis and feline lower airway disease (asthma). It is important to recognize that ongoing therapy is key in achieving successful outcomes in patients with chronic conditions. Conditions such as epilepsy or atopy are controlled, not cured, and chronic airway disease should follow the same treatment paradigm.

To identify the etiology of chronic airway disease, treatable causes of cough and airway inflammation must first be excluded, including *Mycoplasma* or *Bordetella bronchiseptica* infection, cardiac disease with left atrial enlargement and progressive compression of mainstem bronchi, laryngeal dysfunction, parasitic disease, presence of airway foreign bodies, or neoplastic disease.

INFLAMMATORY AIRWAY DISEASE

Glucocorticoids, such as prednisone, are the mainstay of therapy for inflammatory airway disease in small animals. However, oral corticosteroids have significant side effects in dogs, including polyuria/polydipsia, weight gain, behavioral

changes, and hepatomegaly. Cats have shown increased tolerance to the side effects of glucocorticoids, but oral glucocorticoid administration has been associated with a greater incidence of diabetes mellitus and repositol products have been associated with congestive heart failure in cats.¹

Inhaled corticosteroid (IC) drugs are the first-line treatment for humans with asthma and other inflammatory airway diseases and have been proposed as treatment for moderate to severe steroid-responsive lower airway disease in both dogs and cats.

Inhaled β_2 -agonists (eg, albuterol) are also widely used for bronchodilation in humans with asthma, although recent studies have demonstrated increased mortality and decreased therapeutic efficacy associated with frequent use.² Inhaled β_2 -agonists are warranted for management of asthma and associated bronchoconstriction in small animals, which occurs in some cats with airway disease but typically not in dogs.

INHALED GLUCOCORTICOIDS

The primary advantage of ICs is that they avoid or minimize the systemic side effects associated

Inhaled corticosteroids avoid or minimize the systemic side effects associated with oral glucocorticoids while targeting therapy to the lungs.

IC = inhaled corticosteroid

CONTINUES

Can Inhaled Medications Be Systemically Absorbed?



1

A Himalayan receives inhaled medications for treatment of airway disease. Courtesy of Trudell Medical International

The canine and feline nasal cavities are more complex than the human nasal cavity, and aerosolized drugs may readily disperse in the nasal passages of small animals rather than being delivered directly to the lungs. In addition, adults and older children are trained to use inhalers to direct the aerosol to the lungs, so very little (if any) is inhaled through the nose.

In a study of 20 cats that received a nebulized radio-pharmaceutical agent via face mask, Schulman et al demonstrated that the agent was deposited in the lungs in all cats, although deposition in the stomach was also evident in 75% of the cats.³ This would suggest that, contrary to popular belief, some inhaled medications may be absorbed systemically.

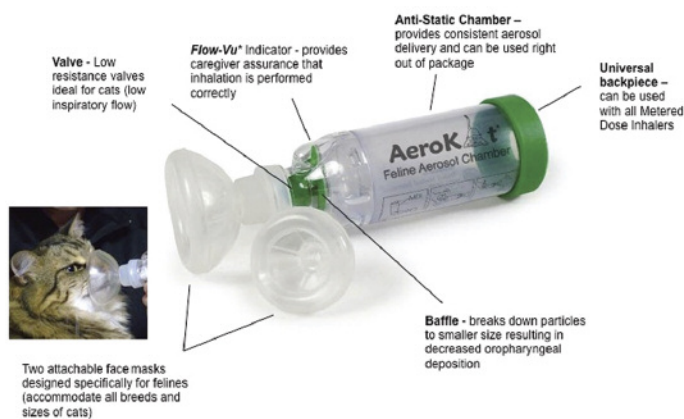
with oral glucocorticoids while targeting therapy to the lungs. In a 2008 study, Cohn and colleagues⁴ showed that IC drugs suppressed the hypothalamic-pituitary axis of dogs but had limited effects on the immune system. IC drugs do increase the risk for diabetes in humans, but the diabetogenic effects of these medications in cats have not been evaluated to date.

Because voluntary cooperation is lacking in pets, administration of IC drugs requires use of a face mask and spacer (Figure 1). Several models are available, but the AeroKat and AeroDawg chambers (trudellmed.com/animal-health) seem to be widely used (Figure 2).

Most pets require a period of acclimation to accept the mask and treatment. In addition, the owner could be exposed to the aerosolized product, although in clinically insignificant amounts.

PREPARATIONS AND DOSING

Several IC preparations are available, including fluticasone, beclomethasone, budesonide, ciclesonide, and mometasone. All IC medications are expensive, and no generic versions are available at this time. Most studies of IC use in small animals have focused on fluticasone.



2

Feline AeroKat Aerosol Chamber delivery device. Courtesy of Trudell Medical International

CFC = chlorofluorocarbon, IC = inhaled corticosteroid, MDI = metered-dose inhaler

The optimum dosing of IC drugs in dogs and cats is unknown. One feline study supported a starting fluticasone dose of 44 mcg Q 12 H,⁵ while another advised 250 mcg Q 24 H.⁶ Anecdotal recommendations for cats include a dose of 110 mcg Q 12 H (to a maximum 440 mcg Q 12 H).

In dogs, starting IC doses of 110 mcg Q 12 H (for dogs weighing up to 10 kg), 220 mcg Q 12 H (10–25 kg), and 440 mcg Q 12 H (>25 kg) may be considered, although no published dosing information is available to support these recommendations.⁷ In both dogs and cats, oral glucocorticoid therapy is typically continued for about 10 to 14 days with a tapering overlap.⁸

IC medications were initially available in metered-dose inhalers (MDI) with propellant chlorofluorocarbons (CFCs), but CFCs have been phased out because of concerns about their effects on the ozone layer. MDIs are now available using other ozone-safe propellants or as dry powder preparations. However, dry powder preparations are not clinically useful in dogs and cats because of the voluntary effort required to utilize them.

Combination products that contain fluticasone and the long-acting β_2 -agonist salmeterol are available; one recent study demonstrated improved efficacy with the use of this product in an experimental model of feline asthma.⁹

THE BOTTOM LINE

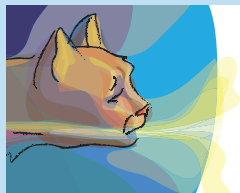
To date, no studies have specifically evaluated the advantages of IC drugs over oral prednisone in dogs or cats with naturally occurring airway disease. However, it is prudent for practitioners to be familiar with inhaled medications.

The advantages of inhaled medications may include fewer systemic effects and complications. It is rare for a cat or dog to respond well to IC drugs if it has not demonstrated clinical improvement with oral steroids. However, if oral steroids are not tolerated or indicated in a particular patient—despite a positive clinical response—transition to IC drugs may be beneficial.

See Aids & Resources, back page, for references & suggested reading.

Teaching Pet Owners About IC Use

It is important that veterinary practitioners become familiar with IC drugs so they can readily discuss the pros and cons of their use with clients. The veterinary team should be able to refer clients to helpful resources concerning IC drug use in pets (particularly cats). One of the best online resources for cat owners is “Feline Asthma with Fritz the Brave!” (fritzthebrave.com), which provides guidelines for the management of cats with lower airway disease.



TRIFEXIS™

(spinosad + milbemycin oxime)

Chewable Tablets

Before using TRIFEXIS chewable tablets, please consult the product insert, a summary of which follows:

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Indications:

TRIFEXIS is indicated for the prevention of heartworm disease (*Dirofilaria immitis*). TRIFEXIS kills fleas and is indicated for the prevention and treatment of flea infestations (*Ctenocephalides felis*), and the treatment and control of adult hookworm (*Ancylostoma caninum*), adult roundworm (*Toxocara canis* and *Toxascaris leonina*) and adult whipworm (*Trichuris vulpis*) infections in dogs and puppies 8 weeks of age or older and 5 pounds of body weight or greater.

Contraindications:

There are no known contraindications to the use of TRIFEXIS Chewable Tablets.

Warnings:

Not for human use. Keep this and all drugs out of the reach of children.

Serious adverse reactions have been reported following concomitant extra-label use of ivermectin with spinosad alone, one of the components of TRIFEXIS Chewable Tablets (see ADVERSE REACTIONS).

Precautions:

Treatment with fewer than 3 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention (see EFFECTIVENESS).

Prior to administration of TRIFEXIS, dogs should be tested for existing heartworm infection. At the discretion of the veterinarian, infected dogs should be treated with ivermectin to remove adult heartworms. TRIFEXIS is not effective against adult *D. immitis*. While the number of circulating microfilariae may decrease following treatment, TRIFEXIS is not indicated for microfilariae clearance. Mild, transient hypersensitivity reactions manifested as labored respiration, vomiting, salivation and lethargy, have been noted in some dogs treated with milbemycin oxime carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

Use with caution in breeding females. The safe use of TRIFEXIS in breeding males has not been evaluated. Use with caution in dogs with pre-existing epilepsy. Puppies less than 14 weeks of age may experience a higher rate of vomiting.

Adverse Reactions:

In a well-controlled US field study, which included a total of 352 dogs (176 treated with TRIFEXIS chewable tablets and 176 treated with an active control), no serious adverse reactions were attributed to administration of TRIFEXIS chewable tablets. All reactions were regarded as mild.

Reactions that occurred at an incidence >2% (average monthly rate) within any of the 6 months of observation are presented in the following table:

Average Monthly Rate (%) of Dogs With Adverse Reactions

Adverse Reaction	TRIFEXIS Chewable Tablets ^a	Active Control Tablets ^a
Vomiting	6.13	3.08
Pruritus	4.00	4.91
Lethargy	2.63	1.54
Diarrhea	2.25	1.54

^an=176 dogs

In the US field study, one dog administered TRIFEXIS experienced a single mild seizure 2½ hours after receiving the second monthly dose. The dog remained enrolled and received four additional monthly doses after the event and completed the study without further incident.

Following concomitant extra-label use of ivermectin with spinosad alone, a component of TRIFEXIS, some dogs have experienced the following clinical signs: *trembling/twitching, salivation/drooling, seizures, ataxia, mydriasis, blindness and disorientation*. Spinosad alone has been shown to be safe when administered concurrently with heartworm preventatives at label directions.

In US and European field studies, no dogs experienced seizures when dosed with spinosad alone at the therapeutic dose range of 13.5–27.3 mg/lb (30–60 mg/kg), including 4 dogs with pre-existing epilepsy. Four epileptic dogs that received higher than the maximum recommended dose of 27.3 mg/lb (60 mg/kg) experienced at least one seizure within the week following the second dose of spinosad, but no seizures following the first and third doses. The cause of the seizures observed in the field studies could not be determined.

For technical assistance or to report an adverse drug reaction, call 1-888-545-5973. Additional information can be found at www.TRIFEXIS.com.

Effectiveness:

Heartworm Prevention:

In a well-controlled laboratory study, TRIFEXIS was 100% effective against induced heartworm infections when administered for 3 consecutive monthly doses. Two consecutive monthly doses did not provide 100% effectiveness against heartworm infection.

In another well-controlled laboratory study, a single dose of TRIFEXIS was 100% effective against induced heartworm infections in a well-controlled six-month US field study conducted with TRIFEXIS, no dogs were positive for heartworm infection as determined by heartworm antigen testing performed at the end of the study and again three months later.

Flea Treatment and Prevention:

In a well-controlled laboratory study, TRIFEXIS demonstrated 100% effectiveness on the first day following treatment and 100% effectiveness on Day 30. In a well-controlled laboratory study, spinosad, a component of TRIFEXIS, began to kill fleas 30 minutes after administration and demonstrated 100% effectiveness within 4 hours. In field studies conducted in households with existing flea infestations of varying severity, flea reductions of 98.0% to 99.8% were observed over the course of 3 monthly treatments with spinosad alone. Dogs with signs of flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatitis/pyodermitis and pruritus as a direct result of eliminating the fleas.

Treatment and Control of Intestinal Nematode Infections:

In well-controlled laboratory studies, TRIFEXIS was ≥ 90% effective in removing naturally and experimentally induced adult roundworm, whipworm and hookworm infections.

NADA #141-321. Approved by the FDA

Manufactured by Elanco Animal Health

A Division of Eli Lilly & Co.

Lilly Corporate Center, Indianapolis, IN 46285

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