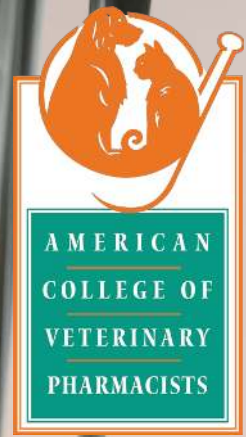


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THE VOICE

OF VETERINARY PHARMACY

SPRING 2021



ACVP 2021 PRESIDENT'S ADDRESS



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We are looking for pharmacy professionals and others allied to the field to provide industry commentary, real world perspective, or news/insight articles related to categories like the following:

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Interested? We strongly encourage writers and representatives to submit your idea in 50 words or less to Linda Cathey, Content Coordinator for The Voice of Veterinary Pharmacy. Linda can be reached at Linda@vetmeds.org.



Keep your eyes on ACVP and get ready for not just an exciting year, but many more to come.



Pg 05 - Don't assume your dog can avoid water danger. Keep an eye on them and give them a hand when needed. Pet tips (your social media tag/handle)



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Emily Yenser,
PharmD Candidate Class of 2023



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ACVP 2021 President's Address

Natalie Young, PharmD, FACVP
PRESIDENT
AMERICAN COLLEGE OF VETERINARY PHARMACISTS

It is an incredible honor to become the President of the American College of Veterinary Pharmacists. From the bottom of my heart, I am truly humbled to follow in the footsteps of Bill Bradley, Calvin Freedman, Gary Wingate, Steve Leafers, Gigi Davidson, and Randy Carr. These remarkable individuals have set the bar very high, and I will give everything I have towards making them proud.

This has been such a tough year for us all and I never envisioned this day being like this. Like so many of you, I miss the little things about these conferences... seeing my pals, taking feverish notes, praying Gigi doesn't call on me to answer a question, making a B-line for Calvin for my annual hug and photo-op, hiding from Carol's camera, and being in awe of just how fast Steve Leafers can go from a lecture, to in his swim trunks by the pool. It's these things that Zoom and virtual platforms can never replicate. But having seen the layout of this year's conference, the lectures, and all the hard work that the ACA/ACVP staff have put into this, I believe we are in for a phenomenal time. Thank you so much for all your determination to make this possible.

With this Presidential speech, I cannot stand here and make promises to you for the upcoming year. Truth be told, the upcoming year will go by so fast and there will be so much work still to do. But what I will promise you is that I will continue to give so much of my heart to the wheels that are already in motion. So many profound things have occurred this year that I am not sure our membership is even aware of.

Gigi, in all of her quote-unquote retirement time, has been working on the criteria that will allow veterinary pharmacists, outside of the teaching hospitals, to become boarded. This will allow our profession the honor and respect it deserves. Susie Bartlemy was able to work her incredible southern charm and deliver two seats to ACVP on the APhA House of Delegate floor. Gigi, along with Brenda Jensen, two of the most respected individuals in the compounding industry, now represent us in those seats. And I watched yesterday as these two texted me with complete school girl glee as history unfolded. APhA gave hopeful consideration to our new business item asking for the term patient to include non-human species. The doors this will open for our profession are tremendous.



I must also mention our student program which is exemplary thanks to the work of many and the leadership of Erika Wassack and Savannah Cunningham. I can guarantee that there are few, if any, organizations with the student enthusiasm ours is cultivating. I've been blown away at each of our virtual student meet-and-greets with our Board. I really don't know how I'm going to hire them all.

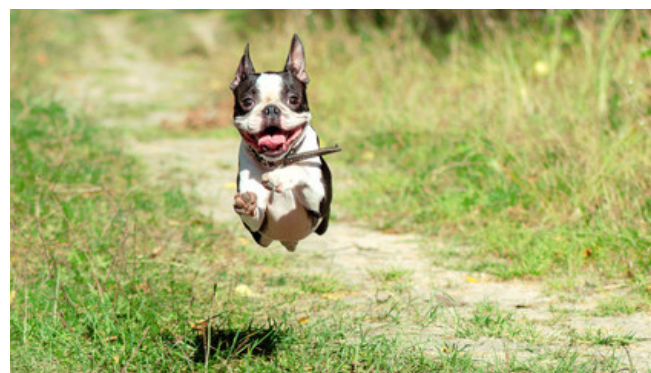
There are so many more things to share with you and I'm excited about them all. I do invite all of you to join our Board meetings and especially our new town halls, to stay informed.

Keep your eyes on ACVP and get ready for not just an exciting year, but many more to come.

And sincerely, with all my heart, thank you for this opportunity.

Media message kit for summer heat and pet safety

As the temperatures get extreme for much of the country, pet safety should be considered. Below are six reminders, including suggested social media messages, to share how people can enjoy the summer with their pet while keeping them safe from seasonal health hazards.



- Respect the heat. Humans aren't the only animals that can find a hot summer day overwhelming. Your pet has a limited ability to deal with the heat. Dogs release heat through their paw pads and by panting, while humans can sweat through all of the skin on their body. Dehydration can be a big problem for pets during the hot weather, too. Signs indicating the discomfort of your cat during hot weather are tremors, vomiting, diarrhea, lethargy, and excessive drooling, etc. You should also keep an eye on elderly or overweight pets or animals with heart and lung disease.

Post: In the summer, make certain Fido and Fluffy always have access to plenty of fresh, cool water, and avoid letting them run around outside during hottest parts of the day. Pet tips from (your social media tag/handle)

- Keep bugs away—safely. Dogs and cats are very susceptible to tick bites and tickborne diseases. Vaccines are not available for most of the tickborne diseases that dogs can get, and they don't keep your pet from bringing ticks into your home. For these reasons, it's important to use a tick preventive product on your pet.

Tick bites on dogs and cats may be hard to detect. Signs of tickborne disease may not appear for 7–21 days or longer after a tick bite, so watch your pet closely for changes in behavior or appetite if you suspect that your pet has been bitten by a tick.

Post: Talk to your vet about the best tick borne-preventative products for you dogs and cats during the summer months. Pet tips from (your social media tag/handle)

- Fertilizers and pesticides may help keep a lawn looking great, but they can be very dangerous for your pet. In the areas where your pets play, it's better to keep the grass cut short to reduce the presence of ticks and other insects. Also keep an eye out for fertilizer warnings on neighbors' lawns when walking your dog.

Post: Be aware and keep pets away from lawn fertilizers. For advice on which ones and how talk to your veterinary. Pet tips (your social media tag/handle)

- Beware of antifreeze. In the summertime, antifreeze can leak out of cars when they overheat, leaving puddles on the ground that your dog and cat can easily lap up and swallow. The sweet taste of antifreeze is tempting to dogs and cats, but when this toxic substance is ingested, it's potentially lethal. Pay attention to your neighbors' cars and puddles on your street, and make sure your pets stay clear of it.

Post: Temps and car engines run hot in the summer. Keep your pet away from cars' antifreeze spills. Pet tips from (your social media tag/handle)

- Find out if your pet needs sunscreen. Some pets, particularly those with short fine hair and pink skin, can be susceptible to sunburn. Talk to your veterinarian about which types of sunscreen are safest on your pet's skin and follow up by routinely applying sunscreen as part of your summer routine. Do not use sunscreen or insect repellents that are not designed specifically for use on animals. The ASPCA says ingesting certain sunscreens can cause drooling, vomiting, diarrhea, excessive thirst and lethargy in pets.

Post: Many pets would benefit from sunscreen – but only the appropriate kinds. Find out which pets and which sunscreens your pet might need from (your social media tag/handle)

- Practice water safety. Even dogs that are strong swimmers could have trouble getting out of a pool or get trapped by ropes and other obstacles. For more risky summer adventures with your dog, like boating, look into a doggie life preserver. It could prove to be an excellent investment for his safety.

Post: Don't assume your dog can avoid water danger. Keep an eye on them and give them a hand when needed. Pet tips (your social media tag/handle)

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CBD Cannabinoid Symposium Now Available on Demand

Both the science and consumer marketplace for CBD and cannabinoids are not just moving rapidly. They are twisting, overlapping and at times taking unexpected detours due to variables like state and federal laws and particularly, the challenge to fully inform the public.

The uncertainties have left pharmacists and the medical community in need of clarity.

The Pharmacists Education on CBD & Cannabinoids Symposium held in March cleared up a lot of this confusion thanks to a host of expert speakers who provided crucial guidance on important legalities, discussed the science behind the chemistry and pharmed dynamics of the compounds, separated which products help certain ailments for patients and reviewed case studies of clinical products' most up-to-date usages.

The 8 sessions were recorded and are now available for you to listen and learn at your own convenience. Earn up to 11 hours of continuing education when you purchase the bundle. Individual sessions are also available on-demand.

The symposium was presented by Pharmacists Public Health Initiatives and supported by Greenwich Bioscience.

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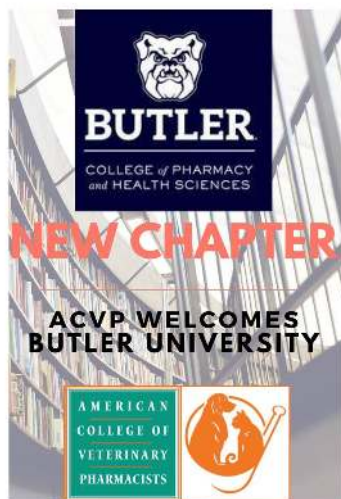
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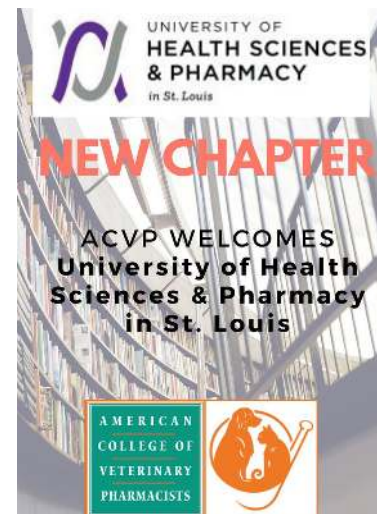
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Separation Anxiety

Emily Yenser
PharmD Candidate Class of 2023
Wilkes University, Wilkes-Barre PA



Introduction

The past year has been unforgettable – filled with isolation and loneliness due to social distancing guidelines and travel restrictions. COVID-19 has kept people away from their loved ones and, for many, away from their work. Since spending more time at home alone has become nearly universal, many individuals have turned to pets – new and old – as sources of companionship. Animal shelters have seen a rise in adoption rates.⁷ Last Chance Animal Rescue located in Maryland, states that their pet adoptions have increased by 30 to 40 percent over the last year.² While this time together is a great opportunity for bonding, pets may begin to experience separation anxiety when routines return to normal and pet owners go back to work.¹ Summer is also a time where many families take advantage of this season to go on vacations, sometimes for extensive periods of time. What people do not realize is how one slight change in routine can place great stress on our pets. Animals cannot ask where we are going or when we will be home. They cannot be comforted by us simply leaving a phone number. Analogous to human behavior, if our animals are inherently worriers by nature, then they are going to worry. Fortunately, there are options to prevent or minimize separation anxiety and its effects.

Pathophysiology

Separation anxiety in any species implies a lack of confidence and an over-dependence on others.³ This condition can affect a variety of species and is not limited to dogs and cats, but for brevity those will be the focal points. At the molecular level, it is hypothesized that adrenocorticosteroids help initiate the long-term stress due to their binding of receptors in the amygdala and possibly other regions of the brain.⁴ The elevation in cortisol levels may be a first step in the progression of physiological changes that promote the development of behavioral problems in shelter dogs and cats.⁴ Serotonin and catecholamines are also involved in the regulation of several behavioral systems that play an important role in the interactions of animals with their external environment.⁵ Dopamine appears to be involved in the expression of active behavioral patterns.⁵

1. Separation Anxiety Presentation

DOGS	CATS
“Accidents” in the home, barking, destructive behaviors, whining, pacing, panting, and salivation ^{6,7,9,11}	Vocalization (crying, meowing), apparent depression, hiding, anorexia, urine marking, excessive self-grooming, claw/scratching of furniture, and hair pulling ³
Follow person from room to room, appear distressed as individual prepares to depart, exuberant greeting behavior during arrival ³	

There are many different causes of separation anxiety. The condition mainly stems from environmental and genetic factors. Environmental causes include separation from family, boredom, inadequate living arrangements, changes to daily routine, a loss or addition of family members or other pets, or a change in residence.^{3,6-8} Orphaned, early weaned, and pet store dogs and cats are at the greatest risk of developing separation anxiety.³ It is also commonly seen in animals from shelters or with single adult owners. Animals at any age can develop separation anxiety, and they need not experience major or traumatic events for this to occur (neglect, abuse, isolation, nutritional compromise, or environmental instability).^{6,9} Genetic factors also play a role and can include emotional sensitivity and a predisposition toward anxiety. Dogs are domesticated from wolves (inherent pack animals) and thus they are especially susceptible to anxiety when isolated. In cats, certain breeds such as Siamese and Burmese may be more prone to developing separation anxiety, while Maine coons have more robust and independent temperaments.³ Dogs and cats are affected by behavioral problems more than any other conditions, often resulting in euthanasia, relinquishment of the pet, or chronic suffering. Problematic behavior is one of the most common reasons that owners rehome their pet, accounting for 47 percent of rehomed dogs and 42 percent of rehomed cats.^{4,10} Most dogs and cats who are brought to shelters, euthanized for behavioral problems, or abandoned are typically around the age of 1 to 3 years old.⁹

Clinical Signs

Separation anxiety can be difficult to recognize as dogs and cats can be particularly good at hiding when they are in distress. Consequentially, pet owners need to be able to be put themselves in “their pet’s paws” and be attentive to their behavior. Not only can the emotional toll significantly impact an animal’s health, but some may even injure themselves in attempts to escape through exit points of their environment, such as windows and doors.⁷ There are signs and symptoms of separation anxiety that pet owners should be aware of and look out for in their animal’s behavior, which are depicted in the chart below. (conti. 11)

Diagnosis

On top of the difficulty to recognize signs of separation anxiety, it is hard to witness this behavior due to it occurring when most people are not home. When it is first suspected, owners should take their pet to see their veterinarian to rule out other medical conditions that could potentially cause abnormal behavior.⁷ A video recording is the most invaluable diagnostic aid to visualize the pet's behavior and determine whether there are other concurrent signs of anxiety.^{6,12} Maintaining a written record (i.e., daily diary) can help identify triggers as well. Diagnosis requires the exclusion of other common causes of the signs. Examples of this are incomplete house training, exploratory play and scavenging, and confinement anxiety.¹² Veterinarians may even take behavioral assessments to track behavioral changes and address problems that arise early in development. Confirming a diagnosis early on is important so that they can educate clients about behavioral problems and risk factors associated with separation anxiety.

Treatment

There are ways to manage separation anxiety in our pets. A comprehensive treatment plan includes behavior modification, environmental enrichment, and minimizing separation to the shortest extent possible.^{6,9} Behavioral modification is defined as, "the systematic approach to change a pet's behavior (including a pet's reaction to a situation, a person, a thing, an animal, etc.)".¹³ Two methods are commonly used to help minimize behavioral symptoms: counter conditioning and desensitization. A chart containing non-pharmacological methods to mitigate separation anxiety associated behavior is provided below.

2. Recommendations to Reduce Separation Anxiety

- Counter conditioning: process of associating the sight or presence of a feared or disliked situation with something the pet enjoys; "special" treat/toy only utilized when owner departs^{7,9}
- Desensitization: process of owner leaving for a short amount of time multiple times per day and then gradually increases the length of these periods with less frequency⁹
- Crate training or confinement using a baby gate⁷
- Daily exercises⁶
- Food dispensing, puzzle toys for mental stimulation^{3,6}
- Referral to certified applied animal behaviorist for cases involving self-injury, aggression, or a lack of improvement in response to other treatment methods⁹
- Referral to certified professional dog trainer for normal but undesired behavior and teaching basic commands^{7,9,13}

Similar to how people are not always capable of managing their anxiety through non-pharmacological methods and must resort to the addition of medications, animals can benefit from pharmacological treatments as well. The treatment options for behavioral conditions like separation anxiety include tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), buspirone, and benzodiazepines (BDZ). For generalized anxiety disorders, SSRIs and TCAs are commonly used. In the United States, two medications are approved as treatment for separation anxiety in dogs: fluoxetine (Reconcile) and clomipramine (Clomicalm).^{12,14} Studies have demonstrated their efficacy when used in combination with behavior modification for treating separation anxiety.^{9,15} Since they require time to work, they are often combined with shorter acting medications (i.e., trazadone, alprazolam, and gabapentin).^{6,16} There are currently no medications available on the market that are indicated for use in cats thus any pharmaceutical used is 'extra-label'.¹⁴ A dosing chart is provided for commonly used anti-anxiety medications in the use of dogs and cats.

Longer-acting anti-anxiety medications (TCAs and SSRIs) may be considered for use if the owners have difficulty predicting departures or triggers.²⁰ Since fluoxetine has been evaluated in and licensed for dogs, it is generally the first choice of the SSRI class, although paroxetine and sertraline may be alternatives when fluoxetine is insufficiently effective or not well-tolerated.^{3,12} This drug class should not be given in conjunction MAOIs due to possible development of serotonin syndrome.¹⁴ An alternative option is the tricyclic anti-depressant class, which is among the most widely and safely used drugs in companion animal behavioral medicine.¹⁷ The parent tertiary amine and the metabolite secondary amine are both useful as treatment options. If a pet is not tolerating a parent compound well, they may do better when treated with the metabolite alone. An example of this is seen with amitriptyline (parent) and nortriptyline (metabolite).¹⁷ Clomipramine and amitriptyline are used most often in this drug class for cats and dogs.^{12,17}





Short-acting anti-anxiety medications can be used when the trigger or departure is known. It can also be used in conjunction with long-acting medications to produce a synergistic anti-anxiety effect.

Diazepam is the most common medication prescribed from the benzodiazepine drug class, but alprazolam and clonazepam are gaining popularity due to their fewer sedating effects.^{12,14,17} This medication is useful when events are triggers for behavior and is normally given as needed with TCAs or SSRIs. For these drugs to be efficacious they should ideally be given at least one hour prior to the anticipated event or minimally before the pet exhibits signs of stress.^{14,17} Buspirone is commonly used for the treatment of behavior disorders associated with fears and phobias and should not be used in combination with MAOIs.¹⁴ Trazadone is used in treating behavioral disorders, particularly in those who do not respond to conventional therapy (SSRIs or TCAs).¹⁴ It is effective in providing short-term relief of anxiety for situations such as veterinarian visits or post-operative confinement.¹⁴ Gabapentin is also a therapeutic option available, although current literature is limited.¹⁹ It appears to be beneficial to decrease fear response and anxiety associated with veterinary examinations.¹⁴ Liquid gabapentin formulations should be cautioned in use with dogs; it commonly contains a sweetener (xylitol) that is toxic, thus a xylitol-free solution must be utilized.¹⁴ When switching between anti-anxiety medications to see which one works best, the medications should be either tapered off or have a 'wash-out' period of about 2 weeks between stopping one and starting another.¹² There are also natural products available to help calm or reduce anxiety. Examples of ingredients include L-theanine, tryptophan, and systemic pheromones. These are rarely helpful when used alone and evidence of efficacy is limited.^{6,9,12} It is important to note that animals should not be scolded or punished during treatment. Anxious behaviors of pets are not the result of disobedience. When treating a pet with separation anxiety, the goal is to resolve the underlying cause through positive experiences so that they can enjoy, or at least tolerate, being alone.¹¹

Conclusion

Before starting any medications, the pet should have normal baseline values taken to ensure normal liver and kidney function since these are the primary organs metabolizing medications. Baseline EKGs are also recommended to provide a reference point because some medications mentioned can increase heart rate (sign of serotonin syndrome) and affect cardiac muscle.^{9,12} Owners should be provided with educational material on the anti-anxiety medication, including information regarding its adverse effects.

Resources that provide pet-specific information include Saunders Handbook of Veterinary Drugs and Plumb's Veterinary Drug Handbook, both of which are accessible online. Client monitoring is important and should include observation of heart rate, sedation, changes in appetite, vomiting, diarrhea, and new behavioral changes.⁹ Continuing to video the pet when home alone will allow the veterinarian and pet parent to see whether there is improvement or not.

Early intervention is essential to preserve quality of life for both the pet and client as well as to provide the best chance of treatment success.⁹ Unfortunately, if this condition is left untreated, behavior tends to worsen. Without intervention the pet's immune system can become compromised and/or they may become severely depressed.^{6,8} This can result in a shortened life-span and increased severity and frequency of skin disorders. There is evidence to suggest that the stress of living with a fear or anxiety disorder can have negative effects on health span and lifespan of domestic animals.¹⁸ Eliminating the cause of the stress or helping the pet handle the situation is key to mitigating the anxiety.⁸ Educating pet owners on proper physical and emotional development may prevent behavioral conditions from occurring and even increase adoption retention.



3. Dosing Chart: Medications for Anxiety

DRUG	DOGS	CATS	MECHANISM OF ACTION	Notable Commentary
Chronic Therapy				
Amitriptyline Human- Elavil	Adjunctive treatment with behavior modification (extra-label): Start with 1 - 2 mg/kg PO every 12 hours x 2-4 weeks. May gradually increase dose by 1 mg/kg as tolerated (max of 4 mg/kg twice daily) ^{11,14}	Adjunctive treatment of behavior disorders (extra-label): 0.5 - 1 mg/kg PO once daily or divided twice daily. Start at lower end of dosing and gradually increase as tolerated ¹⁴	Drug Class: Tricyclic antidepressant Mechanism: TCAs in general work by inhibiting the reuptake of neuronal chemicals, although the exact mechanism is not fully understood. ¹⁴	Formulations (Amitriptyline): 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, & 150 mg tablets. Compounded dosage forms may be available ¹⁴
Clomipramine Veterinary- Clomicalm Human- Anafranil	Separation anxiety (FDA approved): 2- 4 mg/kg PO once daily or divided twice daily ¹⁴ Adjunctive treatment of behavioral condition (extra-label): 1 - 2 mg/kg PO twice daily initially and can increase up to 3 mg/kg PO once to twice daily. For situational anxiety/phobias it's recommended to be used with a benzodiazepine as necessary ¹⁴	Adjunctive treatment of behavioral conditions (extra-label): 0.25 - 1 mg/kg PO once daily. It is often translated into 2.5 - 5 mg/cat PO once daily ¹⁴	Drug Class: Tricyclic antidepressant Mechanism: TCAs in general work by inhibiting the reuptake of neuronal chemicals, although the exact mechanism is not fully understood. ¹⁴	Formulations: Veterinary (Clomicalm): 5 mg, 20 mg, 40 mg, & 80 mg tablets; Human (Clomipramine): 25 mg, 50 mg, 75 mg capsules ¹⁴
Fluoxetine Veterinary- Reconcile Human- Prozac	Separation anxiety in conjunction with a behavior modification plan (FDA-approved): 1 - 2 mg/kg PO once daily ¹⁴ Adjunctive treatment for behavior disorders (extra-label): Label dose of 1 - 2 mg/kg PO once daily has been recommended but doses can be as high as 3 mg/kg every 24 hours ¹⁴	Adjunctive treatment for behavior disorders (extra-label): recommended dosage is typically 0.5 - 1.5 mg/kg PO every 24 hours ¹⁴	Drug Class: Selective Serotonin Reuptake Inhibitor Mechanism: SSRIs work by inhibiting the reuptake of serotonin into the presynaptic neurons without affecting norepinephrine and dopamine. ¹⁴	Formulations: Veterinary (Reconcile): 8 mg, 16 mg, 32 mg, & 64 mg chewable flavored tablets; Human (Fluoxetine): 10 mg & 20 mg tablets; 10 mg, 20 mg, and 40 mg capsules; 20 mg/5 mL oral liquid; can be compounded into transdermal formulations ¹⁴
Adjunctive Therapy				
Alprazolam Human-Xanax	Adjunctive treatment of anxiety disorders or phobias (extra-label): 0.02 - 0.1 mg/kg PO every 6 to 12 hours as needed ¹⁴ Give 30 to 60 minutes prior to expected trigger ¹⁴	Adjunctive treatment of feline anxiety disorders, spraying, and overgrooming (extra-label): 0.125 mg- 0.25 mg per cat every 8 to 24 hours ¹⁴ Give 30 to 60 minutes prior to expected trigger ¹⁴	Drug Class: Benzodiazepine Mechanism: Benzodiazepines work by depressing certain areas of the brain (primarily limbic, hypothalamic, and thalamic) to produce a sedative and muscle relaxant effect. ¹⁴	Formulations (Alprazolam): 0.25 mg, 0.5 mg, 1 mg, & 2 mg regular tablets; 0.25 mg, 0.5 mg, 1 mg, & 2 mg orally disintegrating tablets; 0.5 mg, 1 mg, 2 mg, & 3 mg extended-release tablets; 1 mg/mL oral liquid. Compounded formulations may be available ¹⁴

Bupropion Human-Bupropion	Adjunctive treatment of low-grade anxieties and fears (extra-label): most recommendations fall within 0.5 - 1 mg/kg PO every 8 to 12 hours but 2 mg/kg has been noted as well ¹⁴	Adjunctive treatment of low-grade anxieties, fears, spraying, and overgrooming (extra-label): most recommend 0.5 - 1 mg/kg PO every 8 to 12 hours ¹⁴	Drug Class: Antidepressant Mechanism: This antidepressant acts as a partial agonist of serotonin receptors and as an agonist/antagonist of dopamine receptors in the CNS. ¹⁴	Formulations (Bupropion): 5 mg, 7.5 mg, 10 mg, 15 mg, & 30 mg tablets. Compounded formulations may be available ¹⁴
Diazepam Human- Valium, Diazepam	Situational anxiety (extra-label): Diazepam 0.5 - 2 mg/kg PO as needed (preferably 30 to 60 minutes prior to anticipated event) ¹⁴ In combination with fluoxetine and behavior modification therapy for anxiety (extra-label): Diazepam 0.5 mg/kg PO once daily for 4 weeks ¹⁴	Oral use is not recommended in cats; safer (and more effective) alternatives are available for anxiety, phobias, etc. ¹⁴	Drug Class: Benzodiazepine Mechanism: Benzodiazepines work by depressing certain areas of the brain (primarily limbic, hypothalamic, and thalamic) to produce a sedative and muscle relaxant effect. ¹⁴	Formulations (Diazepam): 2 mg, 5 mg, & 10 mg tablets; 1 mg/mL & 5 mg/mL oral liquid; 5 mg/mL injection, 5 mg/mL rectal gel ¹⁴
Gabapentin Human- Neurontin	10-20 mg/kg PO every 8 to 12 hours ¹⁴	Reduce fear responses and anxiety associated with veterinary examinations (extra-label): 50-100 mg/cat PO ¹⁴	Drug Class: Anticonvulsant Mechanism: It is not fully understood how it works, but it appears to decrease calcium influx by binding to voltage-gated calcium channels. This results in inhibition of the release of excitatory neurotransmitters (substance P, norepinephrine, glutamate) ¹⁴	Formulations (Gabapentin): 100 mg, 300 mg, 400 mg capsules; 600 mg & 800 mg tablets; 50 mg/mL oral liquid. Compounded smaller sized capsules and a xylitol-free oral liquid may be available ¹⁴
Trazodone Human- Desyrel	Adjunctive treatment of anxiety related disorders (extra-label): PRN doses can be given in addition to another serotonergic agent (clomipramine, fluoxetine) and has a typical starting dose of 5 mg/kg (max dose of 14 mg/kg/day) ¹⁴ Give 60 minutes prior to expected trigger ¹⁴	Anxiolytic prior to vet visits (extra-label): In a placebo-controlled trial, cats were given 50 mg/cat PO 60 to 90 minutes prior to the vet visit and saw a significant effect ¹⁴	Drug Class: Serotonin Antagonist Reuptake Inhibitor Mechanism: Acts as an antagonist to inhibit reuptake of serotonin in the CNS as well as histamine and adrenergic receptors ^{14,15}	Formulations (Trazodone): 50 mg, 100 mg, 150 mg, & 300 mg tablets; may be compounded into an oral liquid ¹⁴

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Conflicts of Interest

The author certifies no conflict of interest.

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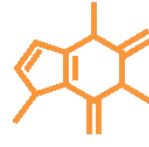
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Working Dogs: Getting the Job Done

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Typically when we think of canines, we envision cute, furry, loving pets that are waiting for us by the door after a long day at the office. They are members of our families, sources of great joy, and sometimes great frustration when they find an old shoe that catches their attention. However, man's best friend may also be man's best co-worker. Since the early 1900's we have been using dogs in a growing capacity to help us with everything from taking down terrorists to helping us cross the road safely. This article aims to shine light on working dogs of different breeds and to discuss how pharmacists can help keep them safe and working in the field. With an increasing number of working dogs, pharmacists are more likely to care for one or more as patients and should be aware of the drug-induced (iatrogenic) side effects that may cause them harm.

History of Working Dogs

Working dogs are those that have been trained to do a specific task and have undergone extensive training with their handler (human counterpart). In the United States, there are an estimated 30,000-50,000 working dogs in active service¹. Working dogs are capable of a growing list of abilities, including drug detection, bomb detection, search and rescue, guide dogs, cancer detection, and assisting individuals with visual impairments.

Although it is hard to pinpoint exactly when working dogs began their extraordinary work, the first seeing eye dog in America was documented in 1928. That year Morris Frank, a blind man living in New York heard about a woman training sight dogs for veterans of World War I in Switzerland. He penned her a letter asking if there was anything she could do to help his situation. She agreed to help, and Morris went to Switzerland to receive handler training with his first guide dog named Buddy². That woman was Dorothy Harrison Eustis. After successfully helping Morris, they founded our nation's first guide dog school, "The Seeing Eye".



During the same time, Dorothy was breeding dogs in Switzerland, the United States military began using dogs in an unofficial capacity during the first World War. In the beginning, military working dogs (MWDs) were used to transport messages between trenches, and also served as a small reminder of home for the troops. In between WWI and WWII, the dog program was essentially abandoned until March 13th, 1942 when these animals were officially commissioned by the U.S Army³.

Today, there are 5 distinctive breeds used as working dogs (German Shepherds, Belgian Sheepdogs, Doberman Pinschers, Collies, and Siberian Huskies). The working dogs do far more than carrying messages in today's world. They are essential team members of the military, the police, and serve as guide dogs for those with sight and hearing difficulties.



Specializations of each Breed

Breed	Average Size (lbs)	Specializations
German Shepherd	65-90	Police K-9, MWD, SAR
Belgian Sheep	55-75	Intelligence, Police K-9, MWD, SAR
Doberman Pinscher	60-90	Protection, Guiding
Collie	60-75	Guide
Siberian Husky	35-60	Cold weather operations

Table 1: Characteristics of the top 5 working dog breeds^{4,5,6,7}

German Shepherds are a common breed of working dogs. They serve as police dogs, military working dogs, and can be used in search and rescue operations as well. This breed is well adapted for these missions because they are calm and approachable but carry themselves with an unmistakable confidence. With a bite force of 238 PSI, they can easily break our bones and can be used to coerce suspects out of hiding in police situations⁴.



Belgian Sheepdogs serve in similar roles as the German Shepherds and are known for their intense level of intelligence. The Belgian Malinois is a member of this family and was a part of the mission that took down Osama Bin Laden. In his book *No Ordinary Dog*, retired Navy Seal Will Chesney details the trials and tribulations that led him and his partner Cairo while serving on one of America's most important missions. These two were more than co-workers – they were true partners, in every way imaginable. Despite being injured on multiple deployments, Cairo maintained the tenacity and courage to get back in the fight to protect his human family of Navy Seals. Every day thousands of MWD's protect our soldiers and serve our country.

Doberman Pinschers can range between 60-90 pounds of pure muscle and historically served as guard dogs. These are the dogs that you would see in movies from the 1990s guarding a junkyard or the bad guys' hideout. Today, they are used in service roles of all capacities including guide dogs for the blind, therapy dogs, and have even been used in search and rescue operations⁵.

Collies are best suited for guiding and assisting their human counterparts. They are extremely well behaved and have an intelligence that pairs well for sight and assisting their partner⁶. These dogs do not like inactivity, and the nature of their service allows them to be very active in assisting. They can pick up dropped items, open doors, and quickly alert their handler of danger that may be ahead. Since they are a herding breed and exceptionally smart, they sense body language cues from their handler and react quickly.

Siberian Huskies are best known for being sled dogs. In the arctic tundra, they may be the only means of transportation and are invaluable to the human inhabitants of this terrain. The snow, cold weather, and huge workload placed on them allow them to burn up all the energy they have. They have been used in arctic military missions in the past and have saved entire towns. In 1925, Nome, Alaska experienced an outbreak of diphtheria and the nearest medical aid was 674 miles away. A sled dog named Balto and his musher Gunnar Kaasen led the team of dogs on this journey, and when a blizzard made sight impossible Balto finished the last 53 miles back home using the familiarity of the trail by scent⁷.

Drug and Bomb Detection

We all know that dogs have a better sense of smell compared to humans, but just how much better? According to a 1999 study done by researchers at Auburn University's Institute for Biological Detection Systems, canines were found to detect compounds at levels of only 500 parts per trillion. When the Alcohol, Tobacco, and Firearms (ATF) agency is training its detection dogs they expose them to chemical compounds found in up to 19,000 different explosive devices. To pass the ATF certification, the K-9 must blindly identify 20 substances, with 2 substances being foreign and not used during training⁸. This federal agency alone has trained approximately 5,200 detection dogs since 1986, and these dogs have saved countless lives. You can find detection dogs at every major port in the United States, both the Northern and Southern borders, and as you are passing through TSA.

In the book *Trident K-9 Warriors*, Mike Ritland a former Navy Seal goes into detail on the training process for MWD's. Mike and his company, Trikos International, have been working to train our nation's



MWD's for 20+ years. By using positive reinforcement (giving treats and playtime with their favorite toys), Mike and his team can train dogs in a variety of tasks. When a dog takes down a suspect or when they find the scent they are training for they get to have their reward. Even when Will Chesney was on deployment with Cairo, he would have his favorite toy at the ready to reward him for a job well done.

Service Dogs

Service dogs are not the same as emotional support animals (ESAs) under the American's with Disabilities Act (ADA)⁹. ESAs are considered companion animals and are used to ease their handler's anxiety, depression, or other hardships they may be experiencing. Service dogs assist individuals with disabilities. Guide dogs can be used to help visually impaired individuals navigate the world safely. The handler and their service partner will undergo approximately 4 weeks of training before they are comfortable enough with each other to go out in the world¹⁰. These guide dogs undergo 2-3 months of training with professionals before being paired with their human. In addition to the dogs' training, handlers must also learn special commands and how to listen to their guide dog. (conti pg 18)

Working Dogs: Getting the Job Done (cont.)

The cost to train service dogs can range from \$45,000-\$60,000. Fortunately, many non-profit organizations assist with pairing handlers and dogs together¹¹.

Search and Rescue (SAR)

Dogs have been used in SAR efforts since the early 1900s. Due to their uncanny ability to detect minuscule amounts of particles in the air they are perfect for the job. SAR dogs can be deployed in natural disasters, assist with locating missing people, or assist with locating the deceased as well (cadaver dogs). Each SAR dog has unique abilities. Some are trained to find a specific scent (scent discriminating), and others can follow a scent of any type (non-discriminating)¹². SAR dogs can also be specifically trained for individualized searches,

such as water only, avalanche only, or rubble only. There are approximately 150-200 SAR dog teams spread across the country, and although the exact numbers of individuals



found each year isn't known they are a valuable tool in the SAR field¹³.

Cancer Detection

Recently, some working dogs have taken on a new type of task. Given their ability to smell and detect small amounts of materials, dogs have been studied by researchers to determine if they can detect cancer and other diseases in humans early enough to be effective. Andreas Mershin and his team at MIT's Center for Bits and Atoms are working to leverage these dogs' abilities to detect cancer compounds. Research from a 2015 study showed that dogs trained to detect prostate cancer were successful using urine samples at 98-99% accuracy¹⁴! Investigators thought that they could program artificial intelligence to do similar work, but to date have not been able to replicate canine ability. There is still much work to be done in this field, but these promising results could lead to less invasive and more cost-friendly testing opportunities.



Pharmacy Considerations

Pharmacists can play an important role in the care of working dogs by closely monitoring their drug therapies. As previously mentioned, Collies are often trained as guide dogs. Approximately 70% of Collies express a genetic polymorphism in the ABCB1-1Δ transporter pump at the blood-brain barrier. Drugs such as avermectins (ivermectin, selamectin, milbemycin, and moxidectin), acepromazine, butorphanol, chemotherapy agents (vincristine, vinblastine, doxorubicin, paclitaxel), and apomorphine cause severe toxicity and death in Collies (and other dogs with the ABCB1-1Δ mutation).

Working dogs begin training at a very early age. Because fluoroquinolones can adversely affect developing cartilage and bone, the package inserts for veterinary-labeled fluoroquinolones indicate that these antimicrobial agents are contraindicated in young dogs during the rapid growth phase. As noted in the table above, most working dogs are large breeds who do not complete growth until they are at least 12-18 months old.

Drug	Use	Associated Toxicity
Corticosteroids	Anti-inflammatory	Visual, Olfactory
Metronidazole	Gastrointestinal disease	Olfactory
Aminoglycosides	Antibiotics	Otic
Vancomycin	Antibiotics	Otic
Benzalkonium chloride	Antiseptic	Otic
Chlorhexidine	Antiseptic	Otic
Detergents	Cleanser / Ceruminolytic	Otic
Salicylate	Cleanser / Ceruminolytic	Otic
Furosemide	Heart Disease	Otic
Cisplatin	Cancer	Otic

Table 2: Iatrogenic toxicities in working dogs^{16,17,18,19,20,21, 22}

Due to the nature of their service, excellent hearing, vision, and olfaction is crucial in working dogs.

Pharmacists can prevent and monitor potential drug-induced side effects that could interfere with the function of these important senses. Unfortunately, because dogs are not able to communicate side effects that they may be experiencing, by the time the animals are examined damage can already be done¹⁵. Due to the cost and time associated with training working dogs, paying close attention to medication regimens is crucial.

A list of medications and their related toxicities is detailed in Table 2, above. While this list is not all-inclusive, it provides some drugs known to specifically affect various senses in working dogs. When pharmacists receive prescriptions for these drugs, it is recommended to consult with the prescribing veterinarian to discuss the risks and benefits of therapy and potentially offer alternatives.

Enrofloxacin at doses of > 5mg/kg/day has been shown to cause blindness in cats due to a genetic polymorphism, specifically ABCG2 which is the p-glycoprotein transporter pump that protects the blood-ocular barrier.

Corticosteroids are undoubtedly useful therapies but can lead to ocular deficiencies such as glaucoma and can interfere with wound healing¹⁵. Thus, they should also be used in caution if ocular injuries are present¹⁷. Metronidazole specifically affects MWDs MWDs and explosive detection dogs by adversely affecting the detection of 2 explosive compounds (ammonium nitrate & trinitrotoluene). Although reversible, it could be devastating if one of these working dogs was on metronidazole and still on active duty due to the dampened olfactory senses¹⁸.

The otic injuries seen with topical use of aminoglycosides, benzalkonium chloride, detergents, and other drugs were found to occur only when the tympanic membrane was ruptured²³. A common cause of non-combat injury to working dogs is otitis externa, which would require the topical agents listed above²³; consequently, the tympanic membrane should be checked and found to be intact prior to using these drugs. Systemic agents that can also cause ototoxicity include furosemide, salicylates, and cisplatin¹⁵. Systemic aminoglycosides also pose an ototoxicity risk if concentrations are elevated for too long.

Conclusion

Working dogs have unofficially assisted humans for hundreds of years, and until recently have gone unnoticed in their professional capabilities. These dogs give their lives to protect our soldiers, to protect us at home, and to guide their handlers safely throughout the world. As a member of the care team, pharmacists can help ensure working dogs enjoy a healthy life both during and after service by monitoring drug therapies to prevent drug-induced damage to crucial senses of vision, hearing, and olfaction.

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