

# Do these Fearful and Aggressive Dogs Need Drugs?

Gary Landsberg, DVM, BSc, DACVB, DECVB-CA  
North Toronto Veterinary Behaviour Specialty Clinic  
Thornhill, Canada

In this seminar Dr. Landsberg will collaborate with a colleague to discuss real cases of canine aggression cases and the selection and use of drugs and natural supplements for these cases. Therefore the summary below provides a brief overview of drug selection and use.

## Pharmacotherapy and canine aggression

When a dog is excessively aroused, fearful, anxious, overly reactive lacking impulse control or “behaviorally abnormal”, psychotropic medications are indicated to improve the problem as well as address the dog’s well-being. However, drugs do not change the relationship with the stimulus; therefore, concurrent behavior modification is needed to desensitize, countercondition and train desirable.

Selective serotonin reuptake inhibitors might be most effective for hyperactivity, aggression, social anxiety, generalized fear and anxiety and panic disorders. Four weeks or longer is generally required to achieve full therapeutic effects. Starting the medication at the time of the consultation allows time for the drug to reach optimal therapeutic effect when the exposure program begins.

Medication might not be required for dogs that can be effectively kept away from fear-evoking situations, provided the dog is sufficiently settled and relaxed. Adjunctive medication to further reduce anxiety especially prior to stimulus exposure might include benzodiazepines, trazodone, clonidine or propranolol, alone or in combination. If effective these drugs might be used several times a day.

## Psychotropic drugs

Selective serotonin reuptake inhibitors (SSRI) are most commonly used in dogs that are behaviorally abnormal, to control reactivity and impulsivity, reduce fear and anxiety and improve trainability as well as address the dog’s behavioral well-being. SSRI’s are selective in blocking the reuptake of 5HT1A into the presynaptic neurons. Fluoxetine and paroxetine might be useful for general anxiety disorders, stabilizing mood, reducing impulsivity and behaviorally pathologic aggression.<sup>1,2</sup> Fluvoxamine and sertraline are other options for social and irritable aggression.

The primary mechanism of action of TCA’s is to block the reuptake of serotonin and to a lesser extent noradrenaline. They also have anticholinergic and antihistaminic effects which may contribute to varying levels of sedation, urine and stool retention. Clomipramine and amitriptyline may be useful in controlling underlying anxiety and impulsivity in aggressive dogs. However, studies have shown no effect of amitriptyline or clomipramine on canine aggression.<sup>3,4</sup>

While antidepressants reach peak plasma levels within hours, reuptake inhibition may induce down-regulation of postsynaptic receptors that are responsible for clinical effects. Therefore, 4 weeks or longer is generally recommended to fully assess therapeutic effects.

Buspirone is a serotonin (5HT1A) receptor agonist and a dopamine (D2) agonist. It is used for mild fear and anxiety. It is non-sedating, does not stimulate appetite, and does not inhibit memory. It takes a week or more to reach effect. Adding buspirone to an SSRI might add to the serotonin pool.

Benzodiazepines potentiate the effects of (GABA), an inhibitory neurotransmitter. They cause a decrease in anxiety, hyperphagia, and muscle relaxation. Most have a rapid onset and short duration in dogs. They can be used alone or adjunctively primarily on an as needed basis but may be considered in select cases on an ongoing basis with multiple daily dosing.<sup>5,6</sup> They may cause paradoxical excitability, increased activity, and an amnesic effect. Buspirone and benzodiazepines can disinhibit fearful and inhibited pets which may result in aggression.

Beta blockers such as propranolol reduce physiologic signs of anxiety (heart rate, respiratory rate, trembling). Therefore they might be most useful if combined with drugs that reduce behavioral anxiety.<sup>5</sup> Clonidine a selective alpha-2 agonist that blocks noradrenaline, might be used together with SSRI’s for situational use in fear or territorial aggression, separation anxiety, or noise phobias.<sup>7</sup>

Trazodone, a serotonin 2A antagonist-reuptake inhibitor, may be useful in dogs for generalized anxiety, separation anxiety, storm phobias, and some forms of aggression including interdog aggression and impulse control disorders. Trazodone can be used on an as needed basis alone or in conjunction with a TCA or SSRI or 2 to 3 times daily.<sup>8</sup>

Focal seizures of the temporal lobe may present with mood alterations or hallucinatory and self-traumatic behaviors. Generalized seizures may be associated with aggression e.g. in the post-ictal phase. Therefore anticonvulsants may be a consideration in diagnosis and treatment. Levetiracetam may be effective for focal seizures, and for anxiety, panic, and mood disorders which may have comorbidity with epilepsy. Gabapentin might be combined with SSRI’s for the treatment of impulse control disorders, noise phobias and to reduce reactivity. Carbamazepine is also a mood stabilizer that may be a useful adjunct to SSRI’s for irritable and impulsive aggression.

Neuroleptics decrease motor function at the level of the basal ganglia in the brain, elevate prolactin levels and may reduce aggression as dopamine antagonists. Phenothiazines such as acepromazine are sedatives but do not reduce anxiety.

Selegiline is an MAOB inhibitor licensed for CDS in North America, and emotional disorders in Europe. Chronic stress associated with stereotypic and displacement behaviors, fear aggression, and autonomic signs, may have elevated prolactin levels, which might improve with selegiline, while lower prolactin levels are seen with acute onset fears and phobias which might improve with fluoxetine.<sup>9</sup>

Complementary and alternative medications are another option; however, few have been assessed in evidence based studies. Products that might be useful in reducing anxiety and improving trainability include Adaptil, alpha-casozepine, L-theanine, melatonin, Harmonase and aromatherapy. Each of these might be used concurrently with drug therapy. Aggression might be reduced by supplementing tryptophan to a reduced protein diet (to optimize entry through the blood brain barrier). In addition, adding tryptophan to an SSRI or TCA may increase the available serotonin pool. Royal Canin Calm diet contains both alpha-casozepine and L-tryptophan. There have been no studies to demonstrate efficacy of other natural products including Bach flower remedies or homeopathy.

### Abnormal aggressive dogs

For most cases of behaviorally abnormal dogs an SSRI such as fluoxetine or paroxetine would be the first choice for managing underlying anxiety and impulsivity. Immediate acting medications might be needed concurrently prior to specific events including benzodiazepines (e.g. alprazolam, lorazepam, diazepam), trazodone, clonidine, or propranolol. Drug combinations may be a consideration but safety and potential for reefficacy must be weighed against potential adverse effects. Natural products might also be used concurrently. In some cases drug combinations will need to be considered such as a combination of SSRI with carbamazepine, gabapentin, clonidine, trazodone, buspirone or even a TCA (with cautious monitoring for serotonin syndrome).

### Drug doses for behavior therapy

	Dose
Alprazolam	0.02-0.1 mg/kg bid to qid
Clonazepam	0.1-1.0 mg/kg bid to prn
Diazepam	0.5-2 mg/kg prn to q6h
Lorazepam	0.25-0.2 mg/kg sid to prn
Amitriptyline	2.0-4.0mg/kg bid
Clomipramine	1-3 mg/kg bid
Citalopram	0.5-2.0 mg/kg sid
Fluoxetine	1.0 – 2.0 mg/kg sid
Fluvoxamine	1.0 -2.0 mg/kg sid – bid
Paroxetine	0.5-2.0 mg/kg sid
Sertraline	1-5 mg/kg sid or divided bid
Clonidine	0.01-0.05mg/kg prn to tid
Propranolol	0.5-3.0 mg/kg bid or prn
Buspirone	0.5-2.0 mg/kg sid-tid
Trazodone	2 to 8 mg/kg prn to tid (up to 15 mg/kg prn)
Gabapentin	10-30 mg/kg bid to tid
Carbamazepine	4-8 mg/kg bid to tid
Levetiracetam	20 mg/kg tid
Selegiline	0.5-1 mg/kg sid in am

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