



# Animal Behavior Case of the Month

## Statement of the Problem

A dog was evaluated because of excessive barking, whining, and drooling and destructive behavior when it was left alone.

## Signalment

The patient was an 11-month-old neutered male Great Dane weighing 47 kg (103 lb).

## History

The dog lived with the owner (a young man) and his mother. It had previously been crate trained, was participating in a positive reinforcement-based training class, and was walked at least twice daily with a head halter. The dog was fed ad libitum. The owner occasionally punished the dog, but his mother did not. The patient had recently been in a dog day-care facility on weekdays and had good behavior when it was there.

The patient's behavior problems began when it was 6 to 8 months old; at that time, the owner stopped coming home for lunch. The dog began to bark in its crate when it was alone; a bark-activated shock collar had been used. At that time, the patient also began to tear up the bed in its crate when it was alone. Then, the owner moved in with his mother; after this, the dog was reluctant to get in its crate and would not eat treats or from food-stuffed toys in the crate. Within 5 minutes after it was alone, the dog began to drool, whine, and bite the crate bars. One time, the dog escaped from the crate, chewed through an interior door, and pulled down drapes in the house. When the owner returned home, the dog was soaked in saliva and shaking. One morning, the mother left while her son was still in bed. Five minutes later, he awoke to find the dog pacing, whining, and scratching at the door through which the mother had left the house. The dog had pulled a few pieces of molding off the walls. After the dog saw the owner, it relaxed. The referring veterinarian prescribed fluoxetine (1.28 mg/kg [0.58 mg/lb], PO, once daily for 8 weeks) prior to referral for a behavioral evaluation.

## Physical Examination Findings and Laboratory Results

At the time of the initial behavioral evaluation, physical examination revealed healing lacerations on

the dog's face that had resulted from destructive behavior when it was alone. The medical record indicated that the dog had previously injured its face and feet when it had damaged the crate. No other abnormalities were detected.

A CBC and serum biochemical analyses had been performed 4 months prior to the behavioral examination. Mild hyperphosphatemia (9.3 mg/dL; reference range, 2.9 to 6.6 mg/dL) and an alkaline phosphatase activity higher than the reference range (155 U/L; reference range, 20 to 150 U/L) were detected, but these findings were expected for a young large-breed dog that was still growing.<sup>1,2</sup> Mild hyperglycemia was also identified (124 mg/dL; reference range, 60 to 110 mg/dL), but this was attributed to a stress response secondary to handling and restraint.<sup>3</sup>

## Diagnosis

Differential diagnoses for each behavior problem of the dog were determined. For whining when the dog was alone, differential diagnoses included separation anxiety, hyperattachment,<sup>4</sup> and noise phobia. For shaking when the dog was alone, differential diagnoses included separation anxiety, hyperattachment,<sup>4</sup> noise phobia, hepatic encephalopathy, and seizures.<sup>4</sup> For excessive drooling when the dog was alone, differential diagnoses included separation anxiety, hyperattachment,<sup>4</sup> noise phobia, hunger, hepatic encephalopathy, and seizures.<sup>4</sup> For destructive behavior when alone, differential diagnoses included separation anxiety, hyperattachment,<sup>4</sup> play, investigative behavior, hunger, noise phobia, barrier frustration, inadequate exercise or stimulation, compulsive disorder,<sup>5</sup> and seizures.<sup>4</sup> The dog had escape and destructive behaviors, had anxiety behaviors, and refused to eat food or treats only immediately after it was left alone. Such behaviors stopped immediately after the owner returned. These behavior patterns and the history of a move and a change in the owner's schedule suggested that separation anxiety was a likely diagnosis,<sup>4-6</sup> whereas play, investigative behavior, hunger, and compulsive disorder were not likely diagnoses. Results of previous blood analyses and the known behavior trigger of perceived owner absence suggested that hepatic encephalopathy and seizures were not likely in the patient. The dog had daily exercise and training; therefore, inadequate exercise was not a likely diagnosis. Barrier frustration was also unlikely because the dog had destructive behavior when it was alone loose in the living area but not when the owner or his mother was perceived to be home. The patient's history did not indicate that noises elicited an abnormal fear response from the dog; therefore, noise phobia was not likely. A diagnosis of separation anxiety was made for the dog.

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## Treatment

The owner was instructed to maintain the dog's daily exercise and training routine, to feed it twice daily, and to refrain from using any punishment.<sup>4,6</sup> Additionally, the owner was instructed to ignore attention-seeking behaviors and avoid casual interactions and instead interact with the dog only in a cue-response-reward format.<sup>4,6</sup> Systematic desensitization was used to retrain the dog to confinement in a crate.<sup>4,6</sup> The owner was instructed to feed the dog, hide treats for it to find, and offer a food-stuffed toy in its crate. After the patient would enter the crate willingly and lie down, the owner was to continue to desensitize it to the additional triggers of shutting the crate door, time in the crate, and their distance from the crate; the owner and his mother gradually increased exposure of the dog to such triggers until they could leave the house momentarily, then for longer time periods. The owner covered the crate with a blanket and put a bed inside the crate during behavior training so that those objects would become safety cues.<sup>5</sup> The blanket and bed were to be removed if the dog had to be in the crate for a long time. Crate confinement is not a routine treatment for dogs with separation anxiety, particularly for those that are anxious about or have a small amount of experience with confinement.<sup>4,7</sup> Crate confinement was recommended for the dog of this report because the amount of destructive behavior had made the owner reluctant to leave it loose in the home. The owner and his mother were to ignore the dog for 20 minutes prior to leaving the house and to give it a food-stuffed toy in its crate without interaction for 5 minutes before leaving. After returning, they were to ignore the dog until it was calm.<sup>4,6</sup> They were encouraged to take the patient to the dog day-care facility as often as possible to avoid leaving it alone during the crate-desensitization process.<sup>4</sup> Fluoxetine (1.28 mg/kg, PO, once daily) was continued,<sup>4,8,9</sup> and clonazepam (0.085 to 0.128 mg/kg [0.039 to 0.058 mg/lb], PO, 1 to 2 hours before departure [minimum amount of time between administration of doses, 8 hours]) was prescribed.<sup>8</sup>

Fluoxetine is a selective serotonin reuptake inhibitor that is used to treat anxiety. That drug has been reported to be efficacious for treatment of separation anxiety in dogs either alone<sup>9</sup> or in addition to behavior modification.<sup>10</sup> Adverse effects of fluoxetine (inappetence, lethargy,<sup>9</sup> vomiting, diarrhea, increased anxiety, or aggression<sup>11</sup>) were discussed with the owner. Benzodiazepines, such as clonazepam, enhance the effect of  $\gamma$ -aminobutyric acid (an inhibitory neurotransmitter) to help control anxiety and panic in humans and dogs.<sup>12-14</sup> Such drugs have a rapid onset of action; therefore, they can be helpful in treatment of animals with emergent behavior and are commonly administered concurrent with selective serotonin reuptake inhibitors.<sup>12,13</sup> Adverse effects of clonazepam (sedation, ataxia, polyphagia, paradoxical excitation, or aggression<sup>12-14</sup>) were discussed with the owner.

## Follow-up

One week after initiation of behavior modification treatments, the dog would eat from a food-stuffed toy in its crate when it was alone but was still drooling

excessively and biting the crate bars when it received clonazepam at a dose of 0.085 mg/kg; however, the dog seemed to drink excessively when it received that drug at a dose of 0.128 mg/kg. Although excessive drinking is not a reported adverse effect of clonazepam, polyphagia or behavioral disinhibition could have caused increased water intake. The owner declined a urinalysis and measurement of water intake for the dog to determine whether it was polydipsic<sup>15</sup>; administration of the high dose of clonazepam was discontinued. We recommended that the owner continue to administer fluoxetine at the previous dose, administer clonazepam at a dose of 0.085 mg/kg, and begin administration of trazodone (1.6 mg/kg [0.73 mg/lb], PO, q 12 h initially; increasing to 3.2 mg/kg [1.5 mg/lb], PO, q 12 h during 1 week).<sup>4,16</sup> Trazodone is an atypical antidepressant classified as a serotonin 2A antagonist and reuptake inhibitor, and it has been used as an adjunct treatment with fluoxetine and benzodiazepines for anxiolysis.<sup>16</sup> Potential adverse effects of that drug (gastrointestinal tract problems, paradoxical excitation, sedation, changes in appetite, and serotonin syndrome<sup>16</sup>) were discussed with the owner.

After the dog received 1 dose of trazodone, it became lethargic and anorectic and developed diarrhea. The referring veterinarian performed a physical examination; results were unremarkable. The clinical signs resolved after the dog was fed a bland diet and trazodone administration was discontinued. Those clinical signs could have been attributable to other causes of gastroenteritis or colitis, such as dietary indiscretion or sensitivity or parasitic, viral, or bacterial infection<sup>17</sup>; alternatively, the clinical signs could have been caused by trazodone. Additional diagnostic tests (eg, fecal analysis, CBC, serum biochemical analyses, or abdominal radiography) were not performed. Other treatment options were discussed with the owner, including administration of a different benzodiazepine (because individual animals have various responses to different drugs of this class<sup>18</sup>). The owner decided to try administration of clonazepam at a dose of 0.128 mg/kg again and did not report a recurrence of polydipsia in the dog.

At the time of the follow-up examination 6 weeks later, the dog weighed 49 kg (108 lb). The owner thought that the dog had a 50% improvement in separation anxiety behavior. The dog had developed fear reactions to noises such as fireworks since the time of the first behavioral consultation. A CD of firework noises was played for the dog at a low volume; the dog stopped, turned, put its ears back, and backed up (ie, had a fear response). Noise phobia was diagnosed for the dog at that time. Systematic desensitization by means of rewarding the dog for relaxed behavior while playing the CD at a low volume followed by gradually increasing the volume was discussed with the owner.<sup>4</sup> Classical counterconditioning by means of giving the dog a food treat immediately following each unanticipated noise was also discussed.

Three months after the initial behavioral evaluation, the owner reported that the dog was having signs of anxiety when the owner or his mother were showering, putting on shoes, or picking up purses; the dog had also started to damage its crate again. The dog weighed

50 kg (110 lb) at that time. The recurrence of the signs of separation anxiety could have been attributable to development of increased owner attachment,<sup>4</sup> development of conditioned fear of the environment because of the concurrent sensitization to noises,<sup>4</sup> or the classical conditioning to departure cues.<sup>5</sup> The owner and his mother were instructed to vary their departure cues and to occasionally perform such cues without leaving the house at various times during each day so that the cues would lose their predictive value.<sup>19</sup> They were instructed to administer clonazepam to the dog at a dose of 0.16 to 0.2 mg/kg (0.073 to 0.09 mg/lb) in accordance with the previous schedule. After the dog had no improvement in its behavior, the owner started administration of L-theanine<sup>a</sup> (2 mg/kg [0.9 mg/lb], PO, q 12 h), an amino acid that is thought to increase release of  $\gamma$ -aminobutyric acid, serotonin, and dopamine in the brain. Results of another study<sup>20</sup> indicate L-theanine may help decrease anxiety-related behaviors. Although no adverse effects of L-theanine had been reported in the veterinary literature at the time of prescribing, the owner was instructed to monitor the dog for possible adverse effects such as changes in appetite or activity level or signs of gastrointestinal tract problems. Two weeks after initiation of L-theanine administration, the owner reported that the dog had become slightly calmer when they left the house. Three months later, performance of a CBC, biochemical analyses, and urinalysis were recommended because the dog had been receiving medications for 6 months.<sup>4</sup> Mild hyperglycemia consistent with an acute stress response (119 mg/dL; reference range, 60 to 100 mg/dL), mild hypoglobulinemia (2.1 g/dL; reference range, 2.3 to 5.2 g/dL), and mild hemoconcentration without related clinical signs (hemoglobin concentration, 18.2 g/dL; reference range, 12 to 18 g/dL; Hct, 55.1% [reference range, 37% to 55%]) were the only abnormalities detected. Because the dog had improvement but still had substantial anxiety associated with going into its crate, we recommended increasing the fluoxetine dose to 1.6 mg/kg. The owner was advised that changes in behavior attributable to the increased dose may not be detectable for up to 4 weeks, and recurrence of previously detected adverse effects was expected. Two months later, the dog was going into its crate on its own to receive its food-stuffed toy and was staying there alone without destructive behavior, drooling, or shaking.

a. Anxitane, Virbac Animal Health, Fort Worth, Tex.

## References

1. Ferguson DC, Hoenig M. Endocrine system. In: Latimer KS, Mahaffey EA, Prasse KW, eds. *Duncan and Prasse's veterinary*

- laboratory medicine clinical pathology*. 4th ed. Ames, Iowa: Iowa State Press, 2003;270–303.
2. Bain PJ. Liver. In: Latimer KS, Mahaffey EA, Prasse KW, eds. *Duncan and Prasse's veterinary laboratory medicine clinical pathology*. 4th ed. Ames, Iowa: Iowa State Press, 2003;193–214.
  3. Evans EW, Duncan JR. Proteins, lipids, and carbohydrates. In: Latimer KS, Mahaffey EA, Prasse KW, eds. *Duncan and Prasse's veterinary laboratory medicine clinical pathology*. 4th ed. Ames, Iowa: Iowa State Press, 2003;162–192.
  4. Sherman BL, Mills DS. Canine anxieties and phobias: an update on separation anxiety and noise aversions. *Vet Clin North Am Small Anim Pract* 2008;38:1081–1106.
  5. Landsberg G, Hunthausen W, Ackerman L. Fears and phobias. In: Landsberg G, Hunthausen W, Ackerman L, eds. *Handbook of behavior problems of the dog and cat*. 2nd ed. Philadelphia: Saunders, 2003;227–268.
  6. Takeuchi Y, Houpt KA, Scarlett JM. Evaluation of treatments for separation anxiety in dogs. *J Am Vet Med Assoc* 2000;217:342–345.
  7. Horowitz DF. Separation-related problems in dogs and cats. In: Horowitz DL, Mills DS, ed. *BSAVA manual of canine and feline behavioural medicine*. 2nd ed. Quedgeley, Gloucestershire, England: British Small Animal Veterinary Association, 2012;146–158.
  8. Landsberg G, Hunthausen W, Ackerman L. Appendix D: drug dosages. In: Landsberg G, Hunthausen W, Ackerman L, eds. *Handbook of behavior problems of the dog and cat*. 2nd ed. Philadelphia: Saunders, 2003;531–535.
  9. Landsberg GM, Melese P, Sherman BL, et al. Effectiveness of fluoxetine chewable tablets in the treatment of canine separation anxiety. *J Vet Behav* 2008;3:12–19.
  10. Simpson BS, Landsberg GM, Reinsner IR, et al. Effects of Reconcile (fluoxetine) chewable tablets plus behavior management for canine separation anxiety. *Vet Ther* 2007;8:18–31.
  11. Crowell-Davis SL, Murray T. Selective serotonin reuptake inhibitors. In: Crowell-Davis SL, Murray T, eds. *Veterinary psychopharmacology*. Ames, Iowa: Blackwell Publishing, 2006;80–110.
  12. Crowell-Davis SL, Seibert LM, Sung W, et al. Use of clomipramine, alprazolam, and behavior modification for treatment of storm phobia in dogs. *J Am Vet Med Assoc* 2003;222:744–748.
  13. Ibanez M, Anzola B. Use of fluoxetine, diazepam, and behavior modification as therapy for treatment of anxiety-related disorders in dogs. *J Vet Behav* 2009;4:223–229.
  14. Crowell-Davis SL, Murray T. Benzodiazepines. In: Crowell-Davis SL, Murray T, eds. *Veterinary psychopharmacology*. Ames, Iowa: Blackwell Publishing, 2006;34–71.
  15. Feldman EC. Polyuria and polydipsia. In: Ettinger SJ, Feldman EC, eds. *Textbook of veterinary internal medicine*. 6th ed. St Louis: Elsevier Saunders, 2005;102–105.
  16. Gruen ME, Sherman BL. Use of trazodone as an adjunctive agent in the treatment of canine anxiety disorders: 56 cases (1995–2007). *J Am Vet Med Assoc* 2008;233:1902–1907.
  17. Tams TR. Gastrointestinal symptoms. In: Tams TR, ed. *Handbook of small animal gastroenterology*. 2nd ed. St Louis: Saunders, 2003;1–50.
  18. Simpson BS, Simpson DM. Behavioral pharmacotherapy. Part II. Anxiolytics and mood stabilizers. *Compend Contin Educ Pract Vet* 1996;18:1203–1212.
  19. Borchelt PL, Voith VL. Diagnosis and treatment of separation-related behavior problems in dogs. *Vet Clin North Am Small Anim Pract* 1982;12:625–635.
  20. Araujo JA, Rivera C, Ethier JL, et al. Anxitane tablets reduce fear of human beings in a laboratory model of anxiety-related behavior. *J Vet Behav* 2010;5:268–275.