Psychopharmacology is the branch of pharmacology that focuses on the effects of endogenous molecules and exogenous molecules (drugs) on behavior. Psychoactive drugs are thought to produce their behavioral effects through their actions on neurotransmitters in the central nervous system. Neurotransmitters are chemicals that, when released by a presynaptic neuron, cross the synapse to stimulate or inhibit the postsynaptic neuron. Neurotransmitters that are particularly pertinent to behavior and behavioral problems are acetylcholine, dopamine, norepinephrine, serotonin, glutamate, and gamma-aminobutyric acid (GABA).

GABA is an amino acid neurotransmitter that is synthesized from glutamate. GABA neurons are primarily inhibitory, are widely distributed in the CNS, and are the site of action of the benzodiazepines and barbiturates.

Acetylcholine is the most widely distributed neurotransmitter. Cholinergic neurons are generally excitatory, with pathways located throughout the central and peripheral nervous systems. Muscarinic cholinergic synapses are found in smooth muscle, cardiac muscle, peripheral autonomic ganglia, and parasympathetic post-ganglionic synapses. Nicotinic cholinergic synapses are found at the neuromuscular junction. Blockade of muscarinic cholinergic receptors is responsible for atropine-like side effects of the antipsychotics and tricyclic antidepressants: dry mouth and eyes, urine retention, constipation, mydriasis, cardiogenic effects (tachycardia), and increased intraocular pressure.

Monoamine neurotransmitters (catecholamines and indoleamines) are related by their chemical structures, are concentrated in the midbrain, hypothalamus, and limbic system, and are stored in granular vesicles within axons and nerve terminals. The principle means of inactivation is by reuptake at the synaptic cleft, and drugs that block or inhibit their reuptake increase their availability and activity.

Catecholamine neurotransmitters (norepinephrine, epinephrine, dopamine) are synthesized from dietary tyrosine and generally produce CNS stimulation. A large portion of the brain’s dopamine is located in the corpus striatum and modulates the part of the extrapyramidal system concerned with coordinated motor activities. Dopamine levels are also high in some regions of the limbic system. Dopamine depletion or inactivation (tranquilizers, neuroleptics, antipsychotics) is associated with behavioral quieting, depression, and extrapyramidal signs. Excess dopamine release (amphetamines, apomorphine, methylphenidate) has been associated with the development of stereotypies.

Norepinephrine is formed from the hydroxylation of dopamine. Centrally, norepinephrine is generally stimulating, affecting learning, memory, and mood. Peripherally, norepinephrine is the
post-ganglionic neurotransmitter of the sympathetic nervous system. Excess noradrenergic activity has been associated with mania, while norepinephrine depletion is associated with depression.

Indoleamines (serotonin, melatonin) are synthesized from dietary tryptophan. Serotonin (5-hydroxytryptamine) receptors are found predominantly in the brain and act primarily in an inhibitory manner both pre- and post-synaptically. Different receptor subclasses are responsible for modulation of sleep-wake cycles, mood, and impulse control.

Monoamine oxidase is an enzyme that metabolizes norepinephrine, dopamine, and serotonin. Monoamine oxidase inhibitors (selegeline) cause elevation in monoamine neurotransmitters by inhibiting this enzyme.

The use of most psychopharmacologic agents in veterinary medicine is extra-label. Therefore, the Animal Medicinal Drug Use Clarification Act (AMDUCA) applies. First, there must be a valid client-patient-veterinarian relationship. For any chief complaint, a complete medical and behavioral evaluation must be conducted. The veterinarian prescribing the medication must personally make the diagnosis and know the scientific rationale for prescribing that drug. This is important to remember, since many individuals representing themselves as “animal behaviorists” make medication recommendations to owners that may or may not be appropriate. In all cases of extra-label medication use, it is the responsibility of the prescribing veterinarian to explain the meaning of “extra-label” to the owner, the reason the medication is being used, and the potential side effects.

At this time, the only FDA-approved uses of psychoactive drugs in animals are Reconcile® (fluoxetine HCl) for canine separation anxiety, Clomicalm® (clomipramine HCl) for separation anxiety in dogs and Anipryl® (selegeline) for canine cognitive dysfunction. All other uses of these medications and all uses of other medications constitute extra-label use. The FDA approval for Reconcile and Clomicalm are specifically for their use in combination with behavior modification. Their use without behavior modification constitutes extra-label use. Psychoactive medications may be helpful as an adjunct to environmental management and behavior modification, and generally should not be used as the sole means of treatment.

The classification of psychoactive drugs into antipsychotics, antidepressants, anxiolytics, and mood stabilizers, is based on their major behavioral effects in humans. When applied to animals, the classifications can be misleading. Nevertheless, since most literature will refer to psychoactive drugs according to this system, it is important to be familiar with it.

In veterinary medicine, the most commonly used medications that are classified as anxiolytics are the benzodiazepines and the azapirones, specifically buspirone. Some medications that are classified as antidepressants also have significant anxiolytic effects in animals and humans and are used in veterinary medicine specifically for their anxiolytic properties.

**Maintenance Drugs, Standing Therapies**

Treatment of chronic conditions, relief of mild to moderate anxiety
Slow onset of action: 4-8 weeks to see maximum effects
Daily dosing for steady state plasma levels
Supportive of behavior modification: may enhance learning

**Event drugs**
Acute onset, fast-acting, situational fears or phobias
Amnestic effects: may interfere with learning
Some have potential for tolerance

**Combination Drug Therapy**
Monotherapy alone is ineffective
Drug combinations may allow use of lower doses
Acute therapy required: maintenance therapy alone may not be sufficient to control phobic reaction during event or early in treatment

Before using combination, consider
Is there underlying logic to using combination?
Is using two together specifically contra-indicated?
Do you increase risk of side effects?

**Primary maintenance drugs**
Selective serotonin reuptake inhibitors (SSRI’s)
Tricyclic antidepressants (TCA’s)
Monoamine oxidase inhibitors (MAOI’s)

**Secondary maintenance drugs**
Azapirone (buspirone)
GABA agonist (gabapentin)
Opioid antagonists (naltrexone)
SARI (trazodone)

**Acute prn therapy**
Benzodiazepine: alprazolam, clonazepam, lorazepam
SARI: trazodone
Alpha 2 agonist: clonidine
Neuroleptics/Tranquilizers: acepromazine

**Benzodiazepines**
Benzodiazepines increase binding affinity of the GABA-A receptor for GABA. The anxiolytic effects are postulated to be due to the action on the limbic system and reticular formation and are distinct from the nonspecific consequences of CNS depression. The primary route of metabolism is hepatic biotransformation. They are highly protein bound (94% protein bound in cats); therefore hypoproteinemia leads to increased volume of distribution. Intermediate metabolites have long half-lives in humans (30-100 hours). Onset of action is quickest for diazepam, lorazepam, and alprazolam.
Side effects may include hyperphagia, muscle relaxation, decreased locomotor activity; possible disinhibition of aggression; paradoxical excitement, increased muscle spasticity, and idiopathic hepatic necrosis. Long-term use in humans can result in neutropenia, jaundice, anemia, and dependence. Regular use of benzodiazepines can interfere with learning and behavior modification programs. There are rare reports of hepatic failure within 3-5 days of starting treatment in cats. Cats do not use glucuronic acid pathways as efficiently as do other species, and extensive binding and/or localization of diazepam and the active metabolite can occur in cats.

Benzodiazepines are used to treat acute fears, anxieties, and phobias, and in cats, for inappropriate elimination and spraying, and as an appetite stimulant. They are often combined with antidepressants for the treatment of phobias.

Drugs and dosages:
Diazepam (Valium®) DOG 0.55 - 2.2 mg/kg po up to tid
Oxazepam: longer duration of action than diazepam; in tolerance and toxicity studies in animals, wider margin of safety than diazepam; DOG 0.2 - 0.5 mg/kg po sid-bid
Alprazolam (Xanax®): high potency, but short-acting; less effect on motor function at low doses than diazepam; DOG 0.25 – 2.0 mg/dog po bid-tid or 0.01 - 0.1 mg/kg po bid-qid; start with 1-2 mg for a 25 kg dog
Clonazepam (Klonopin®): high potency, longer acting, less sedating than diazepam; DOG 0.1 mg/kg po bid-tid

GABA Analogues

Mechanism
Do not alter GABA binding, reuptake, or degradation
Do not serve as a GABA-agonist in vivo
Binds to alpha-2-delta-1 subunit of presynaptic voltage-gated calcium channels, which are upregulated in dorsal root ganglia and spinal cord after noxious insult
Inhibits calcium influx by way of these channels
Inhibits release of excitatory neurotransmitters (substance P, glutamate, norepinephrine) from primary afferent nerve fibers
Inhibits dorsal horn responses to inflammation-induced pain

Gabapentin Indications
Adjunctive therapy for refractory seizures
Chronic pain
Anxiety

Gabapentin Pharmacokinetics
Oral bioavailability (dogs) = 80%
Half-life (dogs) = 3 – 4 hrs
Half-life (horses) = 7 – 8 hrs

In humans, not metabolized
Excreted unchanged in urine
In dogs, significant hepatic metabolism
N-methyl-gabapentin

Gabapentin Doses
Dogs
Seizures: 10 – 30 mg/kg PO q8-12hr
Pain: 10 mg/kg PO q8-12hr (starting dose); 50 mg/kg PO q12hr (max dose)
Cats: 3 – 10 mg/kg PO q12hr

Gabapentin Formulations
Veterinary-labeled: none
Human-labeled
Gabapentin (Neurontin®): 100 mg, 300 mg, 400 mg, 600 mg, 800 mg tablets and capsules

Gabapentin Adverse Events
Sedation, mild
Ataxia
Withdrawal-associated seizures

Gabapentin Precautions
Avoid use of human oral solution
300 mg/ml xylitol
Hypoglycemia, hepatotoxicity

Drug Interactions
Antacids
Hydrocodone
Morphine

**Azapirones (Buspirone, Buspar®)**

Buspirone is a non-sedating anxiolytic drug that is a partial serotonin (5-HT1A) agonist (enhances neurotransmission of 5-HT) and a dopamine receptor agonist and D2 antagonist. Buspirone has a short half-life (2-11 hours). Side effects are uncommon; with mild gastrointestinal upset being most likely. Azapirones cause no significant sedation or muscle relaxation and do not impair motor function or lead to dependence. There is also a low potential for cognitive impairment. Cats may become more assertive during treatment.

Buspirone can be used in the treatment of separation anxiety in dogs, feline urine marking, and for mild chronic fears and anxieties. It may not be effective alone for severe anxiety or panic attacks. It has no anticonvulsant effects.

Buspirone dosages
DOG  1.0 – 2.0 mg/kg po bid–tid; 2.5 – 10.0 mg/dog po bid–tid; 10 - 15 mg/dog po bid-tid for more severe anxiety; 5 mg/dog po bid-tid small dogs; 10 mg/dog po tid big dogs
CAT 0.5 – 1.0 mg/kg po bid; 2.5 – 7.5 mg/cat po bid
Tricyclic antidepressants

As a group, tricyclic antidepressants affect serotonin, norepinephrine, acetylcholine, and histamine. They block the presynaptic reuptake of serotonin and norepinephrine to varying degrees. Tertiary amines (amitriptyline, doxepin, imipramine) are more potent inhibitors of serotonin reuptake, are more sedating, have more anticholinergic and cardiovascular side effects, and are metabolized to secondary amines (desipramine and nortriptyline). Metabolites are more potent inhibitors of norepinephrine reuptake. TCA’s have varying degrees of muscarinic, alpha-adrenergic, and H1 and H2 blocking activity.

TCA’s are well absorbed from the gastrointestinal tract. They undergo demethylation, aromatic hydroxylation, and glucuronide conjugation of the hydroxy metabolite in the liver. Most of the metabolites are also active and are excreted via the kidneys.

The most common side effects seen in dogs are sedation and gastrointestinal upset. Peripheral and central anticholinergic effects can result in constipation, dry mouth, decreased tear production, urine retention, and mydriasis. TCA's can lower the seizure threshold and alter blood glucose levels. In humans, tricyclic antidepressants can cause cardiovascular, neurological, hematologic, gastrointestinal, and endocrine side effects. Testicular hypoplasia has also been reported.

Tricyclic antidepressants should never be used in combination with MAO inhibitors, and should be used cautiously, if at all, with phenothiazines, anticholinergic agents, antidepressants, psychostimulants, anti-thyroid agents, cimetidine, thyroid supplements, and CNS depressants.

Drugs and dosages:

Imipramine (Tofranil®): potent inhibition of serotonin reuptake; potent interaction with alpha-adrenergic, histaminic and muscarinic receptors; Indications: urethral incontinence, submissive urination, narcolepsy, cataplexy; DOG 1.0 – 4.0 mg/kg po sid-bid; start at 1.0 – 2.0 mg/kg bid; 0.5 – 2.0 mg/kg po bid-tid; 5-15 mg/dog po bid; CAT 0.5 – 2.0 mg/kg po sid-bid; start at 0.5 mg/kg bid; 2.5 – 5 mg/cat po bid

Amitriptyline (Elavil®): more potent than imipramine in terms of cholinergic, alpha-adrenergic, and histaminergic receptor blockade; DOG 2.2 mg/kg po bid; 1.0 – 3.0 mg/kg po sid-bid; CAT 0.5 - 2.0 mg/kg po sid-bid; 5 –10 mg/cat po sid; BIRD 1.0 – 5.0 mg/kg po bid

Clomipramine (Anafranil®, Clomicalm™): neurochemically distinct: potent and selective serotonin reuptake inhibition; Indications: anxieties, fears, and phobias, compulsive disorder, hyperesthesia syndrome; DOG 2.0 mg/kg po bid; CAT 0.5 – 1.0 mg/kg po sid

Doxepin (Sinequan®): strong antihistaminic effect; conditions involving pruritis; used in humans with depression, anxiety, and sleep disturbances; DOG 0.5 - 1.0 mg/kg po bid; 3.0 - 5.0 mg/kg po bid-tid; CAT 0.5 - 1.0 mg/kg po sid-bid
Selective serotonin reuptake inhibitors (SSRI’s)

SSRI’s act through highly selective blockade of the reuptake of serotonin at the presynaptic neuron and may facilitate the down-regulation of post-synaptic receptors. Specificity is believed to minimize side effects. Loss of appetite and weight loss may occur. Decreased seizure threshold and altered glycemic control may also occur. Avoid combinations of SSRI’s with MAO-I’s (Anipryl, Amitraz) or other serotonergic drugs (TCA’s), anticonvulsants, and antipsychotics.

Selective serotonin reuptake inhibitors have been used in the treatment of compulsive disorder, offensive aggression, phobias, and anxiety-related disorders.

Drugs and dosages:
Fluoxetine (Prozac®): DOG 1.0 – 2.0 mg/kg po sid
Sertraline (Zoloft®): DOG 1.0 – 4.0 mg/kg po sid-bid; CAT 0.5 – 1.0 mg/kg po sid
Paroxetine (Paxil®): DOG 1.0 mg/kg sid; CAT 0.5 – 1.0 mg/kg po sid

SARI’s, Phenylpiperazines

Serotonin 2 (5HT2A) antagonists (receptor blockade)
Serotonin reuptake inhibition
Alpha-1 adrenergic antagonism
Antihistaminic properties

Trazodone (Desyrel) - Indications
Mild storm phobia
Nocturnal behavior
Adjunctive therapy (SSRI, TCA)


Dose – dogs
2.0 – 8.0 mg/kg PO prn or q12-24hr
Side effects: sedation, gastrointestinal upset

Direct-acting alpha-2, adrenergic agonists

α2-Adrenergic Receptors
Activation of alpha-1-adrenoceptors can functionally antagonize alpha-2-mediated central nervous system (CNS) responses. It is critical to use compounds with high selectivity for alpha-2-adrenoceptor.

α2-Adrenergic Receptors
Noradrenergic neurons: α2-autoreceptors, supraspinal (brainstem) sites, locus ceruleus
Non-noradrenergic neurons: α2-heteroreceptors, dorsal horn spinal cord nociceptive neurons
Clonidine Mechanism
Centrally acting, sympatholytic agent
Direct-acting alpha-2, adrenergic agonist: specificity toward presynaptic α2 receptors in vasomotor center in brainstem, locus ceruleus
Inhibits release of NE

Decrease in sympathetic tone
Reduces sympathetic outflow from CNS
↓ cardiac rate
↓ peripheral resistance
↓ blood pressure
Blocks pain signal transmission to brain
↑ seizure threshold

Uses: High blood pressure, fear/panic

Clonidine Pharmacokinetics
Rapidly and almost completely absorbed after oral administration
Peak plasma level within one hour (oral)
~50% metabolized in liver to inactive metabolites

Clonidine CNS Effects
Sedative/hypnotic: potentiated by benzodiazepines
Anesthetic sparing
Anxiolytic: higher doses can increase anxiety via nonspecific activation of alpha-1-receptors
Analgesic: synergistic with opioids

Clonidine Indications
Fear, anxiety: reduction in stress and anxiety independent of sedative effects
Adjunctive treatment of IBS (cats)
Adjunctive analgesic agent
Pre-anesthetic agent
Hypertension
Glaucoma

Pre-existing stress, fear, excitement can increase circulating endogenous catecholamines and prevent onset of alpha-2 agonist-induced sedation

Clonidine Doses
Dogs: 0.01 – 0.05 mg/kg PO PRN (q12hrs)
Cats: adjunctive antidiarrheal therapy for IBS; 5 – 10 mcg/kg SC or PO q8-12hrs

Clonidine Formulations
Veterinary-labeled: none
Human-labeled: Clonidine HCl (Catapres®): 0.1 mg, 0.2 mg, 0.3 mg tablets
Clonidine Adverse Events
Transient hyperglycemia
Dry mouth
Constipation
Sedation
Aggression
Hypotension
Bradycardia

Clonidine Precautions
Cardiovascular disease
Renal failure

Interactions
Antihypertensive drugs
Beta-adrenergic blocking agents
CNS depressants: Opiates, Barbiturates


Antipsychotics/Neuroleptics/Tranquilizers

Individual antipsychotic drugs show a wide range of physiological effects, with a large variation in side effects. The most consistent effect is dopamine antagonism. They block dopamine receptors in the basal nuclei and limbic system, producing behavioral quieting or a state of decreased emotional reactivity and relative indifference to stressful situations. They suppress spontaneous movements without affecting spinal and pain reflexes. Conditioned avoidance responses are lost in animals that are given antipsychotics. They have anticholinergic, antihistaminic, and anti-serotonergic action.

Antipsychotics are metabolized in the liver, and conjugated and unconjugated metabolites are excreted in the urine. Duration of action ranges from 4 to 24 hours. Antipsychotics are divided into two groups based on side effect profiles. Low potency drugs require larger doses, produce more sedation, anticholinergic side effects, and cardiovascular effects, but have a lower incidence of extrapyramidal motor side effects. The alpha-adrenergic blocking effects result in hypotension, sedation, decreased seizure threshold, and bradycardia. Extrapyramidal motor signs include muscle tremors, motor restlessness, Parkinsonian effects (difficulty initiating movements, motor stiffness, resting tremor, stiff gait, reduced facial movement), and tardive dyskinesia with chronic use. Idiosyncratic aggressive reactions have been reported in dogs treated with single doses of acepromazine.

Antipsychotics are used to treat most forms of psychosis in humans. They do not have the same significance in animal behavior therapy and are used most often for chemical restraint and sedation. They are also used to treat self-injurious and stereotypic behaviors.
The phenothiazine neuroleptics do not have a specific anxiolytic effect. Due to their sedative effects, they are one of the most commonly misused medications in the treatment of behavior problems. They can be useful in preventing damage to the environment and even self-injury by animals with intense fear responses, but they are not appropriate for long-term therapy in the treatment of phobias. Anecdotal evidence suggests that chronic use may result in exacerbation of noise-related phobias.

**Narcotic Antagonists**

Uses: lick granulomas, tail-chasing, other stereotypic behaviors, compulsive disorder

Narcotic antagonists: Mechanisms
Stress (confinement or another event) causes animal to initiate stereotypy. Carrying out the stereotypic behavior causes release of endogenous endorphins, reinforcing the behavior. Narcotic antagonists block the reinforcement.

Side effects: Gastrointestinal effects, especially diarrhea

Naltrexone HCl (Trexan®)
DOGS: 1-2.2 mg/kg q8-12h; CATS: 25-50 mg/cat q24h
PARROTS: 1.5 mg/kg q 12 h

**Recommended Reading**


Hart BL, Cliff KD. Interpreting published results of extra-label drug use with specific reference to reports of drugs used to correct problem behavior in animals. JAVMA 1996; 209(8):1382-1385.


AGGRESSION PROBLEMS IN CATS
Lynne M. Seibert DVM, MS, PhD, Diplomate ACVB

Feline Social Behavior and Communication

Cats are facultatively social, such that their degree of sociality in natural situations depends mainly on the distribution of resources. They are capable of forming stable bonds with other members of the colony and will display positive social interactions with other cats in multi-cat households when relationships are stable. Friendly behaviors consist of allorubbing, allogrooming, sharing space, and group play.

Cats communicate with visual, auditory, and olfactory signals. Head rubbing results in deposition of scent from perioral glands, submandibular glands, and temporal glands. Scratching also results in release of olfactory cues from interdigital glands, as well as leaving a visual mark behind. Both male and female cats can mark with urine, although it is more common for males to spray urine than females. All forms of marking may become more frequent in situations where there are multiple cats housed in a limited area, or if there is social stress present.

Aggression between Cats
Frequent causes of inter-cat social stress or aggression are the introduction of a new cat to the household, fear or redirected aggression following a stressful incident, play aggression, status-related aggression, and medical conditions. For pairs of cats, the longer they have been together, the less overt aggression occurs. This is consistent with the formation of stable dominance relationships that rely on dominance signaling, rather than overt aggression. Introduction of a new cat should always be done gradually and combined with rewards for friendly behavior. The environment should meet the needs of the cats with provision of adequate resources that are accessible for the cats. Scent exchange between the cats can also help facilitate introductions.

Status-related aggression
This problem can occur with cats that have previously established a relationship. The onset of aggression may have an identified event, such as illness of one of the cats, or addition of a new cat that disrupts the social order. The aggressor chases, growls, and attacks other cat or cats, while showing dominance postures, and may also control many of the resources, limiting the other cats’ access to the litter box or preferred resting spaces.

Treatment will require the owner to supervise interactions between the cats and intervene early in the event of escalating dominance challenges; provide additional resources that subordinate cats can access, and possibly the use of medication.

Fear and redirected aggression
A cat that hisses and growls at other cats when they come near while displaying signs of fear (ears back, tails tucked, crouching) is showing fear aggression. Fear aggression can occur between cats that have historically gotten along well together as a result of classical conditioning. Fear-related problems are best addressed using desensitization and counter-conditioning techniques, and possibly medication.
Inter-cat Aggression Instructions
Lynne Seibert DVM, MS, PhD, DACVB

☐ Keep cats physically separated when they cannot be supervised
☐ Avoid all situations that elicit aggression
☐ Increase vertical space: cat trees, furniture, cat perches, scratching posts with perches
☐ Do not attempt to verbally comfort either cat if it is acting fearful or aggressive
  ☐ Instead provide an outlet or escape route
☐ Place a quick-release collar with jingle bells on the aggressor
☐ Flyway diffuser
☐ Videotape interactions between your cats, without allowing them to fight
  ☐ Note staring, ear position, tail position, and stance

Scent Exchange:
☐ Rub a towel all over one cat, especially around the mouth and neck areas, and then rub it all over the other cat, especially around the mouth and neck areas; repeat this activity daily for each cat using the same towel each time
  ☐ If cat dislikes or is afraid of the towel, use a brush or grooming glove
☐ Place grooming combs in common areas to encourage facial marking from the cats

Separation:
☐ Separate cats using a physical barrier
  ☐ Double-stacked child gates
  ☐ Screen
  ☐ Cracked door
☐ Encourage the cats to play with each other under the door, or if possible, through the pet gates
☐ Rotate cats daily so that one cat is confined while the other has free access to the house
  ☐ Provide each cat with food, water and a litter box
  ☐ Provide individualized attention to each cat on a daily basis
  ☐ Separate cats such that stress is decreased and safety is increased
☐ Place food dishes at a distance from the barrier that is acceptable for both cats (both cats will freely approach the food dish and eat without concern or stress)
  ☐ Each day, move both dishes several inches closer to the barrier
  ☐ Provide a special snack for both cats at the same time to encourage them to approach the food dishes at the same time
  ☐ Goal is for cats to eventually eat special treats on either side of the barrier without aggression or fear of the other cat

Behavior Modification:
☐ Interrupt the aggressive cat when it is engaging in pre-aggressive behaviors, at the first evidence of aggression: tail twitch, eye stare, hair standing up, growl, etc.

  1. Interrupt aggressor
□ Loud novel noise
□ Compressed air
□ Never use physical corrections or punishment

2. After interruption, redirect the cat to engage in another activity
   □ Drag a toy on a string away from the other cat
   □ Call the cat to come for a reward

3. If cat cannot be redirected, separate the cats
   □ Reward the aggressive cat if it acts friendly towards the other cat
       Verbal praise       Food treats       Petting

**Gradual Introductions**
□ Find someone to help with this exercise so that each cat has a handler
□ Training sessions should last 10-15 minutes, or as long as the cats are relaxed
□ Find a distance at which both cats can tolerate seeing each other without becoming aggressive or frightened
    o Work on either side of the barrier for safety if necessary
□ Gradual exposure is accomplished using any controlled activity that the cats enjoy
    o Play
    o Grooming
    o Attention, petting
    o Food treats
    o Small amount of canned food
    o Include verbal praise for appropriate behavior
□ Do not attempt to bribe the cats to get them to relax – simply increase the distance between them if they do not appear to be relaxed
□ Gradually move the cats closer to each other as long as they remain calm
□ If either one of the cats hisses, meows or stares at the other cat, back off to a distance where that cat stops these behaviors
Human-Directed Aggression in Cats

Most common diagnoses
- Play
- Fear
- Petting Intolerance
- Redirected Play Aggression

Play Aggression
More likely in young cats
*Usually, but not necessarily, directed toward moving stimuli*
May be directed only to some members of the household
May be a history of using the hands or feet to play with the cat
May be a history of inadequate opportunity for acceptable play
Attacks are often preceded by crouched stalking, staring, tail twitching, i.e. predatory behavior
Ears usually forward, rather than back
While the behavior is play, it can be “vicious” in effect in that the victim is seriously injured with deep puncture wounds from biting and serious scratches from scratching.

Treatment

Avoid situations that elicit the behavior
Enter via a different door
Don’t wear particular clothes that appear to elicit play aggression (e.g. swishing skirts)
Shut cat in own room during particular times and situations when problem is likely to be worse
Provide opportunities for acceptable play
Redirect play: have balls, paper wads, toys, readily available to distract cat when it appears to be in a playful mood

Medication is generally not indicated, although if the aggression is severe, intense, and accompanied by high arousal, the medications used in fear aggression may be useful

Fear Aggression

Postures: ears back, body lowered, tail lowered, avoids person or persons
Context: Aggression occurs when approached, reached for or groomed
Common in feral cats

*May develop via classical conditioning*
- Unconditioned Stimulus (US-event that naturally causes fear)→Unconditioned Response (UR-natural fear response)
- Neutral Stimulus (NS-human, or some characteristic of the human) is paired with the US-→UR
- When the NS is sufficiently associated with the US that it causes fear, the NS has become a Conditioned Stimulus (CS)
Fear, when it occurs in response to the CS is now called a Conditioned Response (CR)

Example: A man wearing a green shirt and a hat is standing near the cat when firecrackers go off and frighten the cat. The cat may discriminate its fear response, e.g. only be afraid of men, or men wearing green shirts, or people wearing hats. Alternatively, the cat may generalize its fear response, e.g. be afraid of all people and anything green.

In house cats, fear aggression may develop for unknown reasons
Genetic predisposition to respond excessively to fear-inducing events
Event may occur which owner is unaware

Treatment
Desensitization and counter-conditioning
Examples:
Drag string that is very long; gradually decrease the length of the string
Roll balls to a sufficient distance that the cat will come out and chase them
Throw treats or lay a treat trail; in either case, make sure there are treats available at a sufficient distance that the cat will approach and eat
Sit near food bowls; set out a bowl of delicious food; sit quietly at a sufficient distance that the cat will approach

If the cat is not afraid of at least one person, that person can sit with the cat and pet it, play with it or give it treats (whatever works best for that cat) while another person whom the cat is afraid sits quietly at a sufficient distance that the cat remains relaxed, playful and/or focused on the food

Medication
Extra-label use for all aggression
Selective Serotonin Reuptake Inhibitor (SSRI’s)
Fluoxetine 0.5 mg/kg PO q24hr
Paroxetine 0.5 mg/kg PO q24hr

Petting Intolerance

If owner initiates petting, cat is aggressive and/or after a certain amount of petting, cat becomes aggressive
When cats groom each other, they groom the head; they do rub each other’s entire body when engaging in allorubbing
Humans, in vigorously stroking cats may be over-stimulating the cat, as well as engaging in interactions that are not species-typical

Treatment
RESTRICT PETTING
Time limit
Aggression usually becomes more likely as the cat is petted for longer and longer periods. Discuss this time frame and only pet the cat for the brief periods that the cat is more likely to tolerate. For example, if the cat is usually OK for less than 30 seconds, but becomes increasingly likely to be aggressive after 30 seconds, the owner should always pet for less than 30 seconds.

Watch for pre-aggression cues
While owners often initially state that the cat “bites without warning,” careful observation of the owner and cat interacting, and/or careful interviewing will usually reveal that incidents are preceded by specific behaviors, e.g. eye stare, skin twitching, tail twitching, restlessness, growling. If the owner does not stop petting on time, as described above, they must stop petting when the cat gives these signals. The cat is, in essence, saying, “I’ve had enough. (Please) stop.”

Owner versus cat-initiating petting
If the cat is worse when the owner initiates petting, they should only pet the cat if the cat solicits petting.

Recommended Reading


Feuerstein N, Terkel J. Interrelationships of dogs (Canis familiaris) and cats (Felis catus L.) living under the same roof. Applied Animal Behaviour Science, 2008;113(1-3): 150-165.


Feline Human-Directed Aggression Worksheet
Lynne M Seibert DVM, MS, PhD, DACVB

Diagnoses: ________________________________
______________________________

**Prevention:**
- Avoid all situations that have elicited aggressive behavior
- Practice threat reduction
  - Do not attempt to pet unless cat solicits attention first
  - Do not corner cat
  - Avoid staring, standing over, sudden movements, petting over the back
- Take precautions to keep individuals protected from injury – wear long sleeves, confine cat away from vulnerable individuals
- Do not interact with cat unless it solicits attention from you first

**Environment:**
- Place bells on a quick-release collar to alert individuals when cat is approaching
- Carry a compressed air can, air horn, whistle, or spray can to interrupt aggressive behaviors when necessary
- Increase vertical space – allows your cat to retreat to a comfortable position
- Offer interactive toys – treat dispensing balls, toys that play back
- Rotate or change toys on a regular basis – provides appropriate outlets for cat
- Maintain a regular schedule: activities in the same predictable order with cat each day, and include play time, set feeding times, and a quiet time

**Medical Evaluation:**
- The following additional tests are recommended for your cat:

**Teach Commands:**
- Perch: going to a designated, elevated perching site
  - Whenever cat gets onto favorite perch spot, say the command, then reward
  - Use treats or catnip to get cat to come to spot, say command, then reward
  - Eventually cat will learn to go to spot on command
- Come: come to owner when called
  - Ask cat to come for a favorite treat (in multiple locations in the house), and say command word as cat arrives, then reward cat
  - Cat will eventually learn to come on command
- Fetch: retrieve and return object that is thrown

**Aggressive Behavior:**
- Interrupt aggressive behavior as early in the behavioral sequence as possible, at the first sign that cat is upset (when cat is engaging in pre-aggressive behaviors)
  - Dilated pupils, tensed muscles, twitching tail, staring, rippling back, body stiffening
- Use a startle tactic, such as a hissing sound, compressed air can, abrupt noise
As soon as the behavior is interrupted, try to engage cat in an activity that is appropriate and will direct its attention – a new game, chasing paper wads, a special treat, or ask cat to obey a command.

If cat cannot calm down, or the aggressive episodes are frequent, either walk away, or give cat a time-out in a quiet area.

Reward cat if it acts friendly towards you:
- Verbal praise
- Food treats
- Toy

Always avoid physical corrections:
- Physical corrections (hitting, kicking, swatting, pushing, pinning your cat, or any other form of physical correction is completely unacceptable, counter-productive, and likely to be dangerous.
- The most effective punishments are quick, calm, non-physical, non-painful startle techniques, such as a shaker can, sudden noise, clapping hands, compressed air.
- To be effective, punishment must immediately follow the undesirable behavior, it must be an appropriate intensity, and it must occur consistently.
- There are very few circumstances in behavior modification where punishment can be used effectively – talk to the doctor before attempting any form of correction.

Desensitization and Counter-conditioning for Petting Intolerance

First identify your cat’s threshold of tolerance for petting:
- Time petting sessions and stop petting prior to an aggressive incident.
- Start petting on the area of the body that does not elicit any aggressive behaviors:
  - Limit petting to the head and neck.
- If your cat hisses, meows, stiffens, flattens its ears, or stares at you at any point during the exercise, decrease the intensity of petting, or discontinue session.
- End petting sessions by standing up and walking away.
- Gradually increase the amount of time you spend petting your cat:
  - Log progress in a journal.
- Gradually increase the amount of petting done away from the head and neck.
- Feed your cat tempting food treats or small amounts of moist cat food, as long as it remains calm for handling.
- Praise your cat for tolerance of petting, along with the food reward.

Desensitization Exercises:
- Engage your cat in an enjoyable activity (play, receiving attention, food rewards).
- Start at the point or distance that is comfortable for your cat.
- Gradually introduce target stimulus, at such a gradual rate that no negative reactions occur and cat remains calm throughout sessions.

Desensitization Exercises:
- Noises
- Strangers
- Children
- ________________________________
Gradually decrease distance between cat and target stimulus, or increase intensity of stimulus
  - Use a toy at the end of a long string – with subsequent play sessions, the string can be shortened and the play can be moved closer to stimulus
  - Food bowl can gradually be moved closer to stimulus
Praise and reward any appropriate behavior

**Products:**
- Feliway diffuser
- Anti-Icky-Poo [www.antiickypoo.com]
- SSSCAT sprayer
- Grooming combs
- Enrichment toys
- Cat furniture

**Medication(s):**
- 
- 

**Additional Instructions:**
TREATING ANXIETY, FEARS, AND PHOBIAS IN DOGS
Lynne M Seibert BS, DVM, MS, PhD, Diplomate ACVB

Anxiety is defined as the apprehensive anticipation of future danger accompanied by somatic symptoms of tension. Fear is a response that prompts an individual to remove or protect it from dangers or noxious stimuli. It has been suggested that fear and anxiety-related behaviors have evolved in order to promote survival in natural environments by enhancing the individual’s ability to avoid danger. For example, fear of thunderstorms leads to hiding behavior that can improve chances of survival in the wild. A phobia is a pathologic state of fear that is amplified beyond the adaptive response and is triggered by a normal environmental stimulus. Phobias are persistent over time, occur consistently with repeated exposure to a stimulus or situation, are irrational or unreasonable given the level of danger present, and usually lead to avoidance of the feared stimulus. Reactions may be intense (catatonia, hysteria, panic attacks).

Fears and phobias may develop because of genetic predispositions, lack of adequate exposure to various stimuli during development, traumatic experiences, or a combination of these factors. Fears and phobias can be debilitating and often require therapeutic intervention.

Fear-related behavior problems seen in dogs include thunderstorm and noise phobias, separation anxiety, fear of people, fear of unfamiliar situations, and fear of other animals. Fear-related problems comprised approximately one-third of all cases in one behavior referral practice and were the most common reason for rejection of potential Guide Dogs in the United States.

Manifestations of anxiety in dogs include panting, salivation, pacing, whining, trembling, destructiveness, excessive vocalization, gastrointestinal upset, anorexia, withdrawal, inactivity, urination, defecation, and self-inflicted injuries.

In veterinary medicine, learning processes play important roles in the development, maintenance, and treatment of anxieties and phobias. Learning is defined as an enduring change in behavior that results from experience with environmental events, but not from fatigue, maturation, or alterations in physiological state. Classical conditioning is a specific learning process that is often at the root of various fears and phobias. In classical conditioning, a neutral stimulus (NS) comes to elicit a response that it would not naturally elicit.

UCS (Unconditioned Stimulus): any stimulus that reliably and naturally elicits a response without prior conditioning
CS (Conditioned Stimulus): a stimulus that does not initially elicit the given response
UCR (Unconditioned Response): response to UCS
CR (Conditioned Response): response elicited by CS

Example:
UCS (Punishment) \( \rightarrow \) UCR (Fear)
NS (Owner) + UCS (Punishment) \( \rightarrow \) UCR (Fear)
NS becomes CS (Owner) \( \rightarrow \) CR (Fear)
Anxieties and phobias can arise from inappropriate, excessive, and unnecessary use of aversive stimuli. This derives from operant conditioning, also called instrumental conditioning, for which learning occurs as a result of the consequences of the behaviors.

In one form of operant conditioning, called positive punishment, the probability that a behavior will recur decreases as a consequence of a stimulus, usually an aversive stimulus, occurring immediately after the behavior. For positive punishment to be effective, the aversive stimulus must occur immediately, be consistent, and be an appropriate intensity for the individual animal. If these conditions are not met, the use of punishment is unlikely to be successful, and the pet may develop classically conditioned fear to circumstances surrounding administration of the punishment (the sight of the owner, the owner frowning, the sound of the owner’s angry voice). Pets that are repeatedly subjected to inappropriate or excessive positive punishment may become afraid in a variety of situations and then become generalized in their fear responses. Postural indications of fear or anxiety include holding the ears down or back, retracting the lip commissure caudally, and panting.

Early experience and genetic predisposition may make some dogs more susceptible to developing anxiety-related disorders. As a result, there is a substantial range in the tolerance of individual dogs to experiencing fear-inducing stimuli. Some dogs will apparently be less affected by harsh training techniques, at least as can be assessed by overt behaviors demonstrating fear, while others will develop chronic fears of various sorts when subjected to such training techniques. Fear-related aggression problems account for the majority of canine aggression cases in behavior practices.

Fear of People

Dogs may exhibit fear of individuals who stare at them, approach them in close quarters, reach over their heads or backs, startle them, reprimand them, or attempt to physically manipulate them. Dogs demonstrate fear with one or more of the following exaggerated submissive postures: ears down or back, forelimbs flexed, tail lowered, body turned away, lip commissure retracted, panting, lip licking, and/or aggression (growling, snapping, or biting). If individuals persist in challenging fearful dogs, they risk provoking aggression. Threat reduction involves avoidance of threatening signals, such as petting on the head, leaning over the dog, and staring at the dog. Individuals should interact with the dog only when the dog solicits attention and is calm.

Fearful dogs should be trained with positive reinforcement for relaxed and confident postures and behaviors. Desensitization and counter-conditioning can be used for specific fears (approaches from strangers, hand gestures, physical manipulations). To use desensitization effectively, you must be able to identify the stimulus that elicits the fear response, and be able to manipulate the intensity of the stimulus so it can be introduced in a controlled, gradual fashion.

Flooding is the term used to describe the deliberate exposure of the animal to a feared stimulus until the response extinguishes or the animal habituates. Flooding is rarely effective and often dangerous. Animals with strong fears may injure themselves or others, or damage their surroundings.
Noise Phobias

Fears and phobias associated with noise are common. Problems severe enough to cause owners to seek professional help occur in up to 20% of dogs. Dogs with storm phobia exhibit both physical and behavioral signs that increase in intensity and frequency as the storm worsens. Behaviors can inflict severe damage to both the pets and their homes. Symptoms include panting, pacing, trembling, contact seeking with owner, hiding, salivation, destructiveness, excessive vocalization, elimination, and self-trauma.

Storm Phobia Treatment

Bring the dog indoors during the storm and provide “white noise” and a safe hiding place, such as a room with no windows or closet. Anxiolytic medication is often indicated. Maintenance medication can be administered daily for the duration of the storm season. Maintenance therapy helps to relieve chronic, mild to moderate anxiety and will have some effect even if the owner is not available to give medication during a storm. Because of classical conditioning, many storm-phobic dogs develop fear of even mild levels of storm-related stimuli. Maintenance anxiolytic options include selective serotonin reuptake inhibitors, tricyclic antidepressants, or azapirones (buspirone). Maintenance therapy alone may not sufficient to control phobic reaction during storm. In combination with maintenance anxiolytic agents, fast-acting medication, such as a benzodiazepines, trazodone, melatonin, or gabapentin, can also be used for acute control of fear.

Behavior modification for noise phobia

Noise desensitization and counter-conditioning will be useful if the dog shows clinical signs during a “mock” storm (recording). Exercises involve positive reinforcement for relaxed behavior during a storm simulation, starting with the least threatening stimuli or lowest volume. The goal of desensitization is for the dog to never experience fear during the exercises.

Separation Anxiety

Separation anxiety is defined as a distress response to separation from an attachment figure. Its prevalence in the canine population is estimated to be about 15-17 percent. It is the second most common presenting complaint in behavior specialty practices.

Clinical signs of anxiety occur when the dog is completely separated from its attachment figure(s). In a study conducted by Flannigan and Dodman (2001), the most common complaint made by owners was destructive behavior in the home during their absence.

The etiology of separation anxiety in dogs is unclear. An attachment disorder has been suspected, however, hyperattachment (excessive contact seeking with the owner) is not a consistent symptom for dogs with separation anxiety. In a study comparing clinically normal dogs with dogs that had separation anxiety, normal dogs were just as likely to follow their owners from room to room as were dogs with separation anxiety. Likewise, dogs with separation anxiety were no more likely to follow their owners around the house than were normal dogs (Parthasarathy and Crowell-Davis 2006). Contact seeking when the owner is at home or being a “Velcro dog” is
not a reliable diagnostic criterion for separation anxiety. The gender of the dog, age when acquired, and presence or absence of other pets in the household does not appear to be significant risk factors for separation anxiety.

Dogs from shelters and dogs adopted as strays may be predisposed to develop separation anxiety, or prove more difficult to treat, but results of data have been equivocal. Dogs with separation anxiety do appear to have a higher reported incidence of noise phobia problems. The onset of separation anxiety often appears to be associated with minor disruptions to the normal schedule: changes to the owners’ work schedules, following boarding or a hospital stay, addition of new family members) and is often reported in geriatric patients with no historical evidence of schedule changes.

The diagnosis of separation anxiety is based on completing a physical evaluation and taking a behavioral history, establishing that the behavioral symptoms are occurring only in the owners’ absence, ruling out other potential causes of the behavioral symptoms (medical conditions, other anxiety conditions, lack of training, lack of environmental management, etc.). Videotaping the dog in the owner’s absence may provide the information necessary for making a diagnosis. Separation anxiety behaviors will occur within a short period after the owners’ departure.

Environmental Management

During the treatment process, it may be necessary for owners to arrange for daycare or pet sitters. Confinement can be dangerous, as many dogs with separation anxiety also suffer from barrier frustration and may injure themselves during escape attempts.

Behavior Modification

Owner attention, reinforcement, and reassurance during departures and arrivals should be minimized. Desensitization and counter-conditioning will involve teaching the dog to exhibit relaxed postures on a cue for rewards. Once the dog has learned to be calm on cue, independence training can be practiced with the dog maintaining a stay command while the owner moves gradually further away for increasingly longer periods.

Many dogs with separation anxiety will display anxiety during the owner’s pre-departure routine (picking up keys, putting on shoes, setting the house alarm). Because the pre-departure cues are temporally associated with prolonged owner absences, these dogs develop classically conditioned fears of the elements of the pre-departure routine. Thus, anxiety begins before the owner ever gets out of the door. Classically conditioned fears can be extinguished by disrupting the pairing of the conditioned stimulus (keys, shoes, alarm) with the unconditioned stimulus (extended absences). This process of extinction can be accomplished if the owners will repeat elements of their pre-departure routine, and stay home instead of leaving (pick up keys and put them down, put on shoes and hang out with dog instead of leaving).

Conditioned inhibition is a technique that can be used to teach anxious dogs to relax during their owner’s absence. These exercises involve using a safety signal (inhibitory conditioned stimulus) during ultrashort practice departures. The safety signal should be a signal that has never
previously been associated with an extended owner absence, and will be presented during brief departures. Over time, as the dog learns to associate this special signal with short, safe owner absences, the length of the practice departure can be gradually extended.

Pharmacotherapy

Due to the intensity of anxiety, the severity of damage that can occur to property, the risk to the patient’s health and safety, and the frequency of exposure to anxiety–provoking owner absences, medication is often indicated to reduce suffering and hasten improvement. There is a variety of anxiolytic medication options available, including two products approved by the FDA for use in dogs with separation anxiety. Medication should always be used in combination with a behavior modification program. The duration of treatment will vary depending on severity and owner compliance with behavior modification. Separation anxiety is a treatable condition, especially with early intervention.
The relaxation exercises are the foundation for further behavior modification.

The purpose is to teach your dog to sit, stay, or lie down, while confident, relaxed, or at least non-anxious, in a variety of situations. The obedience command is not the ultimate goal - it is simply a tool that allows your dog to earn a reward for an appropriate behavior. It also teaches your dog to rely on you for all cues as to the appropriateness of its behavior in a variety of situations.

Since the purpose is relaxation, and not strict adherence to obedience commands, it is important to be able to recognize when your dog is relaxed or confident. It is normal for your dog to turn its ears to the side or back as you reach for it. It is not acceptable for your dog to keep its ears pinned back or held to the side. You must get your dog to bring its ears forward prior to giving the reward. If your dog is reluctant to do this, you will need to become less "threatening." You can accomplish this by avoiding direct eye contact with your dog, crouching or squatting, dropping the reward rather than reaching directly toward the dog, or speaking more softly. If your dog still seems anxious, contact your veterinarian or behaviorist for further advice.

Another postural component of anxiety for dogs is panting, opening the mouth, and/or retracting the lip fold back into a submissive grin. You must get your dog to relax and close the mouth prior to giving the reward.

Your dog's favorite food treat will be used in the exercises. This is a reward or salary - not a bribe. Treats should never be used to bribe a problem dog. Food rewards should be tiny, easily consumed, and highly palatable. They should be given only during exercises so the dog's motivation for them is maintained. Dog biscuits may not provide sufficient motivation, but some foods are so desirable that the dog is too stimulated to relax. Something between the two extremes is preferred.

Teaching "Sit" (and be confident)

Ask your dog to sit. If it will not sit immediately, raise a treat slightly and ask again. Do not tug on the leash, raise your voice, or push it into the sitting position.

As soon as your dog sits, with its ears perked forward, say "good" and give the food treat. The verbal response of “good” should be timed to coincide exactly with your dog perking the ears forward, relaxing the face, and closing the mouth. If your dog jumps up prior to receiving the treat, then withhold the reward, and ask it to sit again. Remember that you are rewarding the behavior or behaviors that are occurring immediately prior to the reward.
Teaching "Stay"

After your dog has mastered sitting with confidence and relaxing, then add the "Stay" command. "Stay" means that your dog should maintain its current posture until you give the release word ("Release" "Free" "OK").

If you ask your dog to stay, and it breaks the stay prior to you giving the release word, do not give the reward. Initially ask your dog to stay for very brief periods. Then gradually request that your dog hold the "stay" request for longer and longer periods.

Always remember that during these exercises, the most important point is that your dog is relaxed and comfortable with the situation. If the dog's ears are up and forward, then proceed. If your dog tends to pin its ears back, or turn them to the side, then back up to an easier (less threatening) exercise.

Incorporate sit-stay exercises into your everyday routine. Ask your dog to sit and stay briefly prior to feeding, going outside, getting attention. The idea is to reinforce appropriate behavior in many different contexts.

Try to work with your dog for short periods (5-15 minutes) on a regular basis. Avoid long training sessions that could result in your dog becoming satiated, bored, or frustrated.

Do several repetitions of each of the following exercises before proceeding to the next.

<table>
<thead>
<tr>
<th>TASK</th>
<th>DATE</th>
<th># REPETITIONS</th>
<th>COMMENTS</th>
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<tbody>
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<td>Sit, stay for 5 sec</td>
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<td>Sit, stay for 3 sec</td>
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<td>Sit, stay for 8 sec</td>
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<td>Sit, stay while you take one step</td>
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<td>Sit, stay while you take 1 step</td>
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<td>Sit, stay while you break eye</td>
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<td>Sit, stay while you take two</td>
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<td>Sit, stay while you walk to the</td>
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<td>Sit, stay while you jump up and</td>
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<td>Sit, stay while you knock lightly</td>
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</table>
Once your dog can maintain relaxed and confident body language for you while you introduce some distractions, and you can easily cue your dog to show confident postures on the 'sit' command, then you can proceed to specific desensitization exercises.

**Separation Anxiety: Behavior Modification**  
Lynne Seibert DVM, MS, PhD, Diplomate ACVB

Separation anxiety is associated with a dog’s inability to remain by him/herself without becoming anxious. Behavior modification for separation anxiety includes two components: 1) Extinguishing the association between pre-departure cues and actually leaving the house, and 2) teaching your dog to remain alone without being anxious.

Extinction of your dog’s reaction to pre-departure cues is easily done. Simply expose your dog to the cues that s/he knows predict your leaving the house, but without leaving the house. For example, you can extinguish your dog’s reaction to your keys jingling by picking up your keys, walking around with them, and putting them down, without actually leaving your home. Repeat this general process with all of the cues indicated below until your dog no longer reacts to them.

Your dog’s reactions to the following pre-departure cues need to be extinguished:

- **Keys**
- Setting the security system
- **Picking up purse/suitcase/bag**
- Bathing/morning routine
- **Putting on shoes**
- Putting on working clothes
- Other: ____________________

After your dog’s reactions to the above cues have been extinguished, s/he is ready to begin safety cue exercises. The following schedule will assist you in teaching your dog to be alone. Some points to keep in mind while you are performing these exercises:

- Use a “safety cue” during graduated departure exercises. The safety cue can be any cue that **has not been previously associated** with your departure (i.e. ring a bell, blow a whistle, leave a special signal). Safety Cue: ____________________

- Go through the process of getting ready to leave during your graduated departure exercises. The practice departure exercises should appear like an actual departure with two exceptions: (1) you will present the safety cue, and (2) you will not actually leave your dog for an extended period of time.

- Do only one (or possibly 2-3) practice departures in a day. Multiple departures in a succession will create anxiety. Practice departures should be done individually, with time in-between for the dog to relax completely.

- Graduated departures should not be done in the morning prior to leaving for work. We want the dog to associate the safety cue with short, safe departures, and practicing with the safety cue in the morning before leaving for work will potentially create a negative association for the cue if the practice occurs too close to the actual long departure.
Initially, you will leave for only a few seconds.

Gradually extend the period of time that you leave during the practice exercises.

Use the following guidelines for increasing the time outside the house:

- Go out to the garage and come back in immediately
- Leave for 10 seconds, 45 seconds, 20 seconds, 60 seconds, 90 seconds, 1 minute, 2 minutes, 90 seconds, etc.

Continue increasing in increments of 5-10 minutes. Consider these numbers to be guidelines only. Some dogs will progress faster than this and some more slowly.

Remember that the goal is to let your dog experience being alone without becoming anxious.

The above refers to time only. You should follow your normal departure routine, e.g. walking out to the car, starting the car, and driving away.

At some point, this will require a steady breakdown of this process, i.e. (1) get into the car, get out and go back in the house, (2) get into the car, start the engine, stop the engine, get out of the car and go back in the house (3) get into the car, start the engine, drive a few feet, stop the car or back it up, stop the car, and go back in the house, etc.

Always remember to use the safety cue ONLY during practice departure exercises – NEVER when you must leave for an extended period of time.

As you increase the length of the practice departures, you can use the safety cue during longer absences.

Over time, with multiple short practice departure associated with the cue, your dog should begin to see the cue as a signal that you will not be gone long, and will look different when the cue is in use. S/he will look expectant and less anxious when the cue is used.

Once your practice departures last 2+ hours, you can increase the length of your absence by 30 minute to 1-hour increments and continue to use the safety cue.

If at any point, your dog shows anxiety, back up to an easier step. You never want to push your dog to the point that s/he becomes anxious.

Provide the safety signal ONLY during training sessions. If you use the safety signal during an actual departure, it loses its value to your dog.

Remember that the “safety signal,” which will be presented to your dog during training sessions ONLY, needs to be removed when you are done with each training session. This signal tells your dog that you will return. Be extremely careful that you do not use the safety
signal when you are going to leave at times other than training sessions—if your dog is exposed to the stress of a complete departure with the safety signal present, you will have lost the meaning of the signal and will need to start over with a new one.
Treatment for Noise Phobia
Lynne Seibert DVM, MS, PhD, Diplomate ACVB

- Neither punish nor comfort your dog when (s)he shows fear
- Purchase a CD or make a tape of meaningful sounds [www.dogwise.com, Sound Sensibilities series, Sounds Good series, or go to download appropriate sounds]

- Determine whether or not your dog reacts to the CD
  Try several different CD’s and a moderate to high volume
  Watch for trembling, hiding, panting, or ears placed back

Desensitization and counter-conditioning for thunderstorms

1) Start by playing the noise CD at a volume that does not cause any reaction in your dog
2) Use ___________________________ to counter-condition your dog
3) Gradually increase the volume to the next level, but avoid eliciting a fear response; go slowly
4) If your dog shows fear when you increase the volume, and does not quickly relax, decrease the volume to the previous level
5) Try to have a counter-conditioning session at least once a day
6) Record the date and duration of the session and the maximum volume reached
7) Describe your dog’s behavior during the session

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<thead>
<tr>
<th>Date</th>
<th>Duration</th>
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<th>Dog’s Reaction</th>
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NUTRACEUTICALS AND SUPPLEMENTS FOR BEHAVIOR PATIENTS
Lynne M Seibert DVM, MS, PhD, DACVB

DRUG
FD&C Act defines drugs, in part, by their intended use: articles intended for use in diagnosis, cure, mitigation, treatment, or prevention of disease; or articles (other than food) intended to affect structure or function of the body of man or other animals.

DIETARY SUPPLEMENT is a product taken by mouth that contains a "dietary ingredient" intended to supplement the diet. This could include vitamins, minerals, herbs or other botanicals, amino acids, enzymes, organ tissues, and metabolites. Dietary supplements constitute a special category under the general umbrella of "foods," not drugs. According to the Dietary Supplement Health and Education Act (DSHEA) of 1994, they do not need approval from FDA before they are marketed, and they do not have to provide evidence to substantiate safety or effectiveness before or after they are marketed.

NUTRACEUTICALS are non-drug substances produced in purified or extracted form and administered orally to provide agents required for normal body structure and function with the intent of improving health and well-being of animals. The North American Veterinary Nutraceutical Council defines nutraceutical as a food or food product that provides health and medical benefits.

HERBS are plants or plant derivatives or extracts prescribed for health or healing
1. Any plant used for culinary or medicinal purposes
2. Leafy plant without a wooden stem
3. Plant with aerial parts that do not persist from one year to the next

Tryptophan

Tryptophan is an essential amino acid. The body uses tryptophan to help make niacin, serotonin, and melatonin. Studies have shown mixed results with respect to tryptophan's effectiveness as a sleep aid in normal patients. Some positive results in humans have been shown in the treatment of conditions typically associated with low serotonin levels in the brain: as an antidepressant alone, or as an augmenter of antidepressant drugs.

Dietary protein
Most protein diets are low in tryptophan and high in large neutral amino acids. Low protein, high carbohydrate diets have an altered plasma ratio of Trp:LNAA, which effects competition between Trp and LNAA for a common BBB transporter mechanism.

DeNapoli JS, Dodman NH, et al. JAVMA 2000;217(4):504-508
Diets fed: LP (18%), or HP (30%)
With and without tryptophan supplementation
Aggression scores highest for dogs fed unsupplemented high protein diets
Effect of dietary protein content and tryptophan supplementation on dominance aggression, territorial aggression, and hyperactivity in dogs

Eosinophilia-Myalgia Syndrome
EMS is a complex systemic syndrome with inflammatory and autoimmune components that affects the skin, fascia, muscle, nerve, blood vessels, lung, and heart. Symptoms include severe muscle pain and abnormally high numbers of eosinophils. The disease has presented itself only in people taking the amino acid L-tryptophan. A tryptophan-related outbreak of EMS (eosinophilia-myalgia syndrome) occurred in 1989, with over 60,000 illnesses, 1500 cases of permanent disability, and 30+ deaths. The problem was traced to L-tryptophan supplied by Japanese manufacturer producing a contaminated batch. Sixty different impurities were identified in lot.

Tryptophan was banned from sale in the US in 1991. Even when the contamination was discovered and the purification process fixed, FDA maintained that L-tryptophan is potentially unsafe. In February 2001, FDA loosened the restrictions on marketing (though not on importation), but still expressed the following concern: "Based on the scientific evidence that is available at the present time, we cannot determine with certainty that the occurrence of EMS in susceptible persons consuming L-tryptophan supplements derives from the content of L-tryptophan, an impurity contained in the L-tryptophan, or a combination of the two in association with other, as yet unknown, external factors."

5-Hydroxytryptophan (5-HTP) is a tryptophan metabolite that readily crosses the blood-brain barrier, but is rapidly decarboxylated by liver to serotonin (5-HT), and is therefore converted to 5-HT before it can reach the brain. It can produce increased blood serotonin levels, which may cause diarrhea and heart problems, while only slightly increasing brain serotonin.

Serotonin syndrome is characterized by autonomic instability, vomiting, diarrhea, tachycardia, hyperthermia, tachypnea, fever, mydriasis, neuromuscular signs, and altered mental state. Serotonin syndrome can occur with combinations of drugs that …
- Facilitate synthesis of 5-HT
- Increase presynaptic release of 5-HT
- Inhibit reuptake of 5-HT into presynaptic cell
- Inhibit metabolism of 5-HT
- Facilitate action of 5-HT at post-synaptic cell

L-theonine
Amino acid contained in green tea
Structural analogue of glutamate
Competitive inhibition of glutamate receptors
Treatment of anxieties and phobias in cats and dogs

Antioxidants
Free radical oxidative damage
Byproduct of oxidative metabolism
Result from stress, disease, age
Damage to cell membranes

Key factor in age-related cognitive decline
Brain especially susceptible to oxidative damage
   - High metabolic rate
   - High lipid content
   - Limited regeneration

Antioxidants
   - Scavenge free radicals
   - Protect biological membranes

Vitamin E (tocopherols)
Vitamin C
Selenium
β-carotene
Flavonoids, carotenoids
Fruits and vegetables

**DIETARY THERAPY**

Antioxidants
Mitochondrial cofactors
Acetyl-L-carnitine
Phosphatidylserine
Anti-inflammatory agents
Omega-3 fatty acids

Hills B/D
   • Improvements in learning/memory
   • As early as 2-8 weeks
   • Aged dogs fed B/D combined with environmental enrichment
   • Significantly increased BDNF mRNA
   • Better able to complete cognitive tasks compared to controls

**Phosphatidylserine**

Phospholipid found in cell membranes
High percentage in brain and at synapses
Facilitates membrane-dependent neuronal processes

Enhances acetylcholine release
Inhibit loss of muscarinic receptors
Activate synthesis and release of dopamine
Neuroprotective: improves memory, learning, and social behavior in dogs and cats
S-ADENOSYL METHIONINE - (SAMe)

Endogenous molecule
Synthesized by liver as well as cells throughout body
Formed from methionine (amino acid) and ATP
SAMe synthase: enzyme manufactured by the liver

S-adenosyl methionine- importance

SAMe essential for major biochemical pathways and metabolic reactions
  • Transmethylation
    Activation and elimination of drugs
    Phospholipid synthesis
    Cell membrane function
  • Trans-sulfuration
    Conjugation reactions used in detoxification
  • Aminopropylation

Production of substances with anti-inflammatory effects
Protein and DNA synthesis

Glutathione precursor
  Cell detoxification and metabolic processes
  SAMe converted to glutathione
  Conversion to glutathione may be deficient with liver disease
  Exogenous SAMe increases liver and red cell glutathione levels

Antidepressant Effects
  Increased serotonin turnover
  Increases dopamine and norepinephrine levels

No contraindications
  Adverse effects minimal to non-existent
  No drug interactions
  Serotonergic agents
  Additive serotonergic effects

S-adenosyl methionine Pharmacokinetics
Pure SAMe unstable and highly reactive
Commercially available oral forms of SAMe are salts
  Sulfate
  Tosylate
  Butanedisulfonate
Oral bioavailability dependent on salt used to stabilize SAMe

Presence of food in gut can significantly decrease absorption
Administer on an empty stomach
1 hour before feeding

S-adenosyl methionine - Doses
18 - 20 mg/kg PO daily dose rounded to nearest tablet size (dogs)
200 mg/cat PO daily dose

**MELATONIN**

Neuroendocrine control of photoperiod-dependent molting
Stimulates winter coat growth
Spring shedding occurs when melatonin decreases
Increases serum prolactin levels, growth hormone, and GHRH
Oral and implantable pineal gland hormone

Melatonin

Produced in pineal gland
Important for circadian rhythms
Receptors in hypothalamus, cerebellum, pineal body

Derivative of 5-HT

Shift opposes 5-HT

Free radical scavenger
Dopamine - inhibiting

Melatonin – possible indications

**Dermatology**
Alopecia X
Canine pattern baldness
Seasonal flank alopecia
Mink industry

Ferrets
Adjunctive therapy for adrenal disease

**Behavior**
Sleep cycle disorders
Cats, geriatric dogs
Phobias
Separation anxiety
Reproduction
  Improve early breeding and ovulation rates
Melatonin - precautions

Humans
  Hepatic disease
  Cerebrovascular disease
  Neurological disorders
  Dysregulation of diabetes
  May potentiate the effects of benzodiazepines

Non-humans
  Pregnant
  Sexually immature
  May effect sex hormone production and fertility
  Side effects are rare when administered orally to dogs

Melatonin - dosages

Behavioral conditions
  3 – 12 mg/cat PO q12 – 24 hrs
  3 – 6 mg/dog PO q12 – 24 hrs
  0.1 mg/kg PO q8 hrs
Dermatologic conditions
  3 – 6 mg/dog PO q8 – 12 hrs
  3 – 12 mg/dog PO q8 - 24 hrs
  3-mo trial before adjusting dose

Pheromone Therapies

Pheromones
  Nonvolatile, bioactive compounds
  Activate vomeronasal organ sensory neurons
  Regulate social behaviors and neuroendocrine release

Commercially available pheromone products
  Synthetic analogue of feline facial pheromone
  Structural analogue representing the appeasing maternal pheromone in dogs


Aromatherapy

Anxiety reduction in humans
- Lavender
- Chamomile
- Sandalwood

Enhance cognitive function
- Peppermint
- Jasmine
- Rosemary

- Aromatherapy for Health Professionals, 3\textsuperscript{rd} edition. Shirley Price, Len Price, 2007
- www.pacificinstituteofaromatherapy.com

Aromatherapy for travel-induced excitement in dogs
Wells, Deborah L, JAVMA 2006; 229(6):964-967

N=32 dogs
Each dog exposed to car rides with owner
  - No odor introduced (placebo)
  - Ambient odor of lavender (5 ml of lavender oil sprayed with diffuser onto sterile cloth)

Dependent measures
- Movement
- Walking, running, jumping
- Standing
- Sitting
- Resting
- Vocalizing

Significant effect on overall behavior (P<0.001)
Dogs exposed to lavender spent
  - Significantly more time resting and sitting
  - Significantly less time moving and vocalizing

Influence of olfactory stimulation on the behaviour of dogs housed in a rescue shelter

Increased resting, decreased barking
- Lavender
- Chamomile

Greater activity, vocalization
Peppermint
Rosemary

**BACH FLOWERS**

Spring water infused with wild flowers
Either by sun-steeped method or by boiling
  27% grape based brandy as a preservative
  Apple cider vinegar
  Vegetable glycerin
  Red shisho extract

Dr Edward Bach (1886-1936)
System of 38 flower remedies that corrects emotional imbalances

Flower essences
  Work through principle of vibrational resonance
  If animal needs the remedy, the remedy will act
  If remedy is not correct, there will be no effect
  Cannot overdose on Bach flower essences
  No effect of dilution

No more than eight essences in combination
Administered orally
  2-4 drops
  3-4 times per day, for 2-6 weeks
  Aerosol spray, or on the skin

**RESCUE REMEDY**
Star of Bethlehem – Orithogalum umbellatum
Rock Rose – Helianthemum
Cherry Plum – Prunus cerasifera
Impatiens – Impatiens gladulifera
Clematis - Clematis vitalba

Combination of Bach Flower Remedies
For traumatic situations, tension, stress, emergencies, situations where we suddenly lose balance mentally
Aids relaxation and focus

**HERBAL REMEDIES**

Valerian (*Valeriana officinalis*)
Kava (Piper methysticum)
Passion flower (*Passiflora incarnata*)
St. Johns Wort (Hypericum perforatum)
Ginkgo (Ginkgo biloba)

Herbal anxiolytics have ill-defined mechanisms of action
Use with caution, or at all, in combination with pharmaceutical anxiolytics

Ginkgo biloba
- Inhibits monoamine oxidase A and B
- Increases dopamine levels
- Phosphatidylserine-like activity

In humans
- Improve short-term memory and cognitive function

Precautions - Herbs

- Patients taking MAO-I’s or anticholinergic agents
- Clotting disorders
- St. Johns Wort
- Photosensitivity
- Activation of CYP450 enzymes

Acupuncture

Pressure-applying garments

Comparison of the effectiveness of a purported anti-static cape (the Storm Defender®) vs. a placebo cape in the treatment of canine thunderstorm phobia as assessed by owners’ reports

N = 13 (storm cape)
N = 10 (placebo cape)

Owners in both groups reported less hiding behavior by the fourth use

Storm Defender®
- 70 % report improvement in global assessment score
Placebo cape
- 67% reported improvement in global assessment score
After fourth use of cape
No statistically significant difference between Storm Defender® and placebo cape