

Protocol for using behavioral medication successfully

If your veterinarian has recommended that your dog or cat be treated with behavioral/psychotropic medication, there are a number of issues with which you should be comfortable prior to and during the treatment with this medication. These issues are discussed below by topic and will help you to successfully use medication as part of an integrated program of behavioral modification and environmental management. This topic list is based on common client questions and on points vets always wish to ensure their clients understand.

Some of these topics are discussed in some depth and the science is explained in layman's terms. If you do not wish to understand how these drugs work, skip these parts and move on to the ones that may be more of a concern for you (e.g., the section on potential side effects).

Key points with which you should be familiar are noted by: **** and you should read these.**

If you still have questions by the time you have read carefully through this protocol, please ask your veterinarian! The better you are able to monitor your dog or cat, the more helpful information you can provide to your vet, so please ask questions as soon as you have them.

Medication has made a huge difference in the quality of the lives of tens of thousands of pets and their human companions. The better your knowledge, the more successful treatment is likely to be. A good dialog with your vet and, or a specialist will help you in this treatment partnership. Good luck!

1. 'Extra label' or 'off label' medication v. that with a dog or cat label:

All the medications prescribed for pets for behavioral problems are available for use for humans with the analogous conditions. That said, most medications used for pets are used 'extra label'. This means that in the USA the FDA has not approved their use for the specific conditions for which they are used in treatment of pet animals. ***This does not mean the medication is unsafe.*** It ***does*** mean that the medications have not undergone the lengthy clinical trials in dogs/cats with targeted behavioral conditions needed to submit an application for dogs/cats to the FDA. Such applications take years to get approved and unless a company thinks it can financially benefit from a veterinary label - especially if generic compounds are available 'extra label' - they are unlikely to be willing to pursue this costly and lengthy exercise. This is why so many drugs used to treat cancer in pets are also prescribed 'extra label'. 'Extra label' use means that the medication can legally be prescribed for the equivalent use it would have in humans. Medications tested and approved for humans almost always have toxicology data obtained from dogs on file.

Currently, medications **with a veterinary label** are available for treatment of behavioral problems in dogs in the USA: Anipryl® (generic = selegiline) for cognitive dysfunction (Pfizer), Reconcile® (generic = fluoxetine) for separation anxiety and Clomicalm® (generic = clomipramine) for separation anxiety (Novartis). These medications have labels for other

conditions and for cats in some countries outside the USA, and such uses are ‘extra label’ in the USA. While there is no difference in biological effect between a brand name medication for dogs and a generic one, there may be differences in cost, size of tablet or capsule, formulation (e.g. tablet, capsule, chewable tablet) that may be an issue for some pets. Understand these differences and, in collaboration with your veterinarian, make the best choice for you and your pet.

2. Potential toxicity:

For many of the behavioral medications we know a lot about potential toxicity in dogs at and above routine dosage ranges because dogs are the models for human toxicology studies of these medications. Much of the toxicology and toxicity data is either published or available from the company or from poison control centers (in the USA: <http://www.asPCA.org/Pet-care/poison-control.aspx>; 1.888.426.4435), should an untoward event occur. Please remember that *ingesting their human’s medication* is the most common reason why pets become toxic from medication.

3. Rare side-effects:

While we do not know the full range of side effects that could be experienced by canine or feline patients treated with these medications, we know what the potential side effects may be. Because licensing trials are small compared to the number of people ultimately treated, this same situation occurs in humans who take these medications. Because we cannot know all of the side effects that could occur, the pharmacological industry participates in ongoing reporting of side effects. Rare side effects may not be detected until tens of thousands of similar patients are treated.

This means that you should be familiar with common side effects and immediately ask questions when you are not sure if you are seeing a side effect. No dedicated veterinarian or specialist minds being asked if some behavior is a side effect of treatment, even if you think that you will sound foolish or silly. Treatment of behavioral conditions with medication requires that we stop worrying about how we sound and do what’s in the best interest of our furred friends.

****** Rare side effects which may require stopping the medication include neurological changes that don’t go away in a day (e.g., staggering, falling over, increased sensitivity to noise, crossed eyes, an inability to sleep or rest, et cetera). Anything that **you** think is really weird should be reported to your vet immediately. If your vet is not available, call the emergency number ASAP, and be willing to bring your dog or cat to an emergency clinic. While highly, highly unlikely, **in the event of a serious side effect, quick action is key**, and the more familiar you are with how to approach the situation, the less you will worry.

When your veterinarian prescribes medication, he or she will provide you with office and emergency phone numbers. Put these numbers somewhere accessible (e.g., taped to the telephone or entered into an automatic speed dial/address book).

- If you have a pet sitter you should always have these numbers near the phone that the pet

sitter will use or entered into his or her cell phone. Review all of your vet's contact information with your pet sitter.

- If you board your pet you **must** insist that the caretakers know about the medication, are able to administer the medication, and have the numbers to call if they are the least bit concerned about any of the pet's behaviors.
- Always make sure you have the name of the medication and the amount your pet takes available. Veterinarians go on vacation and temporary veterinarians may not be able to find medication records quickly.

**** Important point: Emergencies, while rare, can happen.**

Write your vet's daytime and emergency phone numbers here:

Daytime:

Emergency:

Medication (e.g., amitriptyline):

Dose (e.g., 25 mg every 12 h):

In the USA, the ASPCA's poison control center can be reached at: <http://www.aspca.org/Pet-care/poison-control.aspx>; 1.888.426.4435.

4. Relatively common behavioral side effects: The most common of the side-effects for any behavioral medication include the following:

- sleepiness or sedation that wears off in a day or 2,
- gastrointestinal upset that usually shows up as some mild diarrhea or some mucous in the stool,
- changes in appetite that are minor,
- licking of the lips after giving medication with increased belching or occasional vomiting,
- increased water consumption that requires you to fill the dish more frequently,
- deeper sleep,
- changes in pupil size without problems with vision,
- increased heart rate, and
- associated increased panting.

The only side effects that should cause real concern are those that last more than a few days. To minimize and monitor these side effects there are a number of actions you can take.

- Your dog or cat may always drink a little bit more because many of the medications used can cause a dry mouth. This complaint is less common in dogs and cats than it is in

humans, but ensure that you start the day with full, fresh bowls of water. Watch how much your pet drinks. If you think your cat or dog is hanging over the water dish and is excessively thirsty, measure the amount he drinks (amount put in bowl at time 1– amount left at end of day at time 2 = amount consumed in you have 1 pet), and talk to your vet.

- Try giving the medication in food - really good food - like cream cheese, ice cream, peanut butter, yogurt, tinned liver pate paste, et cetera. This will minimize any stomach upset, and stop most of the lip licking and vomiting. These medications are bitter, and it's the taste that causes these effects.
- Clomicalm®, the TCA licensed for use as an aid in the treatment separation anxiety in the USA, and Reconcile®, the SSRI used for the same canine condition, are made palatable by flavoring so that it can be chewed or swallowed. This is one of the biggest benefits of formulation for cats and dogs.
- If your dog or cat experiences mucousy or loose stool, and it doesn't resolve in 3-5 days, consider using a coating agent (kaolin) before giving the medication.
- If you think your pet is sedated, chart the amount of time your pet spends asleep, noting the number of naps, and whether you think the pet is truly 'awake' when he wakes up. If you do this for a few days you will have good data that will suggest whether sedation is a problem and you can discuss your concern with your vet.
- If you think that your pet is experiencing an appetite change, keep a log of how much he eats, when he eats, how long it takes him to eat and any new behaviors associated with eating (e.g., trying to bury his food). After a week you will have enough information to discuss your concern with your vet.

**** Important point:** Most of the medications used to help treat behavioral problems are bitter. If the pet chews through the capsule or tablet, they will salivate profusely and try to chew/lick the substance off. If this happens you may never get your pet to take another capsule or tablet. Consider putting the medication in a terrific treat that the pet will swallow at once to minimize the bad taste and tummy upsets.

The only potentially serious concern listed above is an increased heart rate. Have your veterinarian teach you how to take your dog's or cat's pulse or heart rate.

- If your pet is thin and likes to be handled, you can take the heart rate by putting your hand on either side of her chest under the arms. You'll feel the heart. Count the number of beats in 30 seconds and multiply by 2, or the number in 60 seconds. This is the heart rate.
- You can measure the pulse on bigger or fatter animals by taking the femoral pulse - pressing on the major vein in the back leg. If your pet is calm you can probably run your hand over the middle of the inner thigh and find the femoral vein. Or, your veterinarian can show you how to do this if your pet is calm enough to allow it, or can teach you to take the pulse on a calm dog and you can learn how to take your pet's pulse at home

when she is calmer.

Normal rates can be 60-100 beats per minute depending on the breed and age of dog. Cats have higher heart rates than do dogs. It's important that you know what *normal is for your pet before starting medication*. It's best to take your pet's pulse for a few days while he or she is sleeping or relaxing. This will give you some idea of the range of 'normal' for your animal. Then, after you have started the medication, take the pulse for a few days while the pet is sleeping. ***Big differences should be reported to your vet ASAP*** (e.g, 70 to 140 beats per minute). Small changes generally normalize after a few days (e.g., 70-80 beats per minute).

If your pet seems uncomfortable and continuously pants, regardless of the change, **call your vet, please.**

**** Important point:** Side effects, especially those concerned with increased heart rate, that are dramatic or that do not go away in a few days are problematic. If this happens or if you think your pet is uncomfortable in any way after starting the medication, call your vet immediately. The solution may be to change medication, decrease the drug, or tincture of time, but the key to the best outcomes is a teamwork approach based on shared information!

5. Commonly used drugs/medications. Most of the medications prescribed for the treatment of behavioral problems in pets will fall into one of a few classes:

- benzodiazepines (BZD) and related medications like gabapentin,
- tricyclic antidepressants (TCAs),
- selective serotonin reuptake inhibitors (SSRIs) and serotonin 2A antagonist/reuptake inhibitors (SARIs),
- combination TCAs / SSRIs (often called NaSSRIs for noradrenaline/selective serotonin reuptake inhibitors),
- NMDA inhibitors, like memantine,
- some alpha-adrenergic agonists, like clonidine,
- monoamine oxidase inhibitors (MAO-Is), and
- some newer antipsychotic agents, which will not be discussed here.

With the exception of clonidine, these compounds all act by altering levels of neurotransmitters in certain regions of the brain. They do this either by affecting activity at a neuronal receptor, or by changing the neuron's activity or metabolism by directly altering internal chemistry, or by some combination of actions. See Figure 1 for a cartoon sketch of what a neuron looks like and how it can be affected.

Benzodiazepines:

BZD work by changing the relationship between neurons that are excited/stimulated and those that are slowed/inhibited. BZD increased the neurochemical gamma amino butyric acid

From: Overall KL. *Clinical Behavioral Medicine for Small Animals*, Mosby, St. Louis, 1997 and Overall KL. *Manual of Clinical Behavioral Medicine for Dogs and Cats*, Elsevier, St. Louis, 2013.

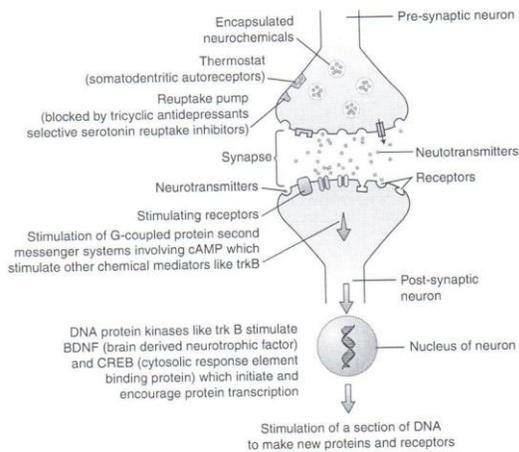
(GABA), an inhibitory neurochemical. This means it slows down or inhibits neurons that would otherwise have been stimulated. In the case of BZD, this effect is part of a balancing act: GABA is made from an excitatory amino acid that acts as an excitatory neurotransmitter, glutamate. You can think of the effects as those involved in a seesaw.....as glutamate increases, the patient becomes very excited, and then as GABA increases, the effect of inhibition becomes more apparent and the patient calms (see figure 2).

The effects from BZD are relatively non-specific effects, meaning that everything calms or everything becomes excited. This is why BZD are not commonly used as daily medications, except in cases of profound panic. BZD also have 3 levels of effects depending on dosage:

- at high levels they act as true sedatives,
- at intermediate levels they act as anti-anxiety medications, and
- at low levels they have general calming effects.

When we use BZD as part of a multi-level behavioral treatment program we are looking for either the calming or anti-anxiety effects. Different types of BZDs have different thresholds for these different effects and affect different receptors to get the desired effect.

Figure 1: Schematic of how neurons work and how these medications affect neurochemicals and receptors



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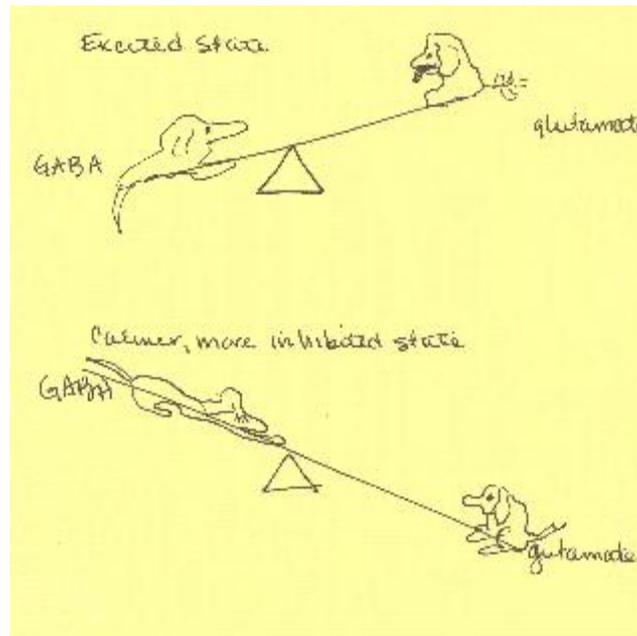


Figure 2: The relationship between glutamate, an excitatory amino acid that stimulates neurons and GABA, an inhibitory neurotransmitter that calms neurons. BZD stimulate GABA.

Please note, cats can have a very rare but *weird, paradoxical response to BZD*: they can become extremely agitated and excited. If this happens, stop the medication and call your veterinarian, please. Dogs can also have an excitation effect but it rarer for them than for cats, and generally less extreme.

**** Important point:** If your pet is taking a BZD and is sedated, sluggish, or really out of it for

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more than a day or 2 - call your veterinarian! This is an undesirable side effect that can usually be managed by changing the amount or type of medication your pet is given.

Do not think that one drug in this class is the same as any other drug. Each medication differs. Your pet should have *only* the dose and medication your vet prescribed: ***not your medication, not one you think is the same, and not a dose that would be easier for you to give.***

If giving the medication at the suggested times in the suggested amounts is hard for you, *talk to your veterinarian* - you will be able to find a regime that works without risking the health of your pet or the good treatment effects.

BZDs include diazepam (Valium in the USA), alprazolam (Xanax in the USA), clonazepam (Klonopin in the USA), and clorazepate (Tranxene in the USA), among other medications.

Almost all of the BZD are abusable by humans. Dogs and cats do not have opposable thumbs and so cannot abuse these medications without human help because they cannot open the bottle at will. Accordingly, ***there are households into which these medications should not be placed.*** Do not be surprised if your veterinarian asks questions about ***household risk.*** Children, pre-teens, and teenagers also have friends which can change the risk. If your household is one that cannot have BZD-type drugs - there are alternatives. Discuss this with your veterinarian.

For some dogs with non-specific anxieties or for those who could benefit from GABA stimulation but may not need a BZD, gabapentin may be a good choice. Gabapentin looks like GABA and so stimulates the same pathways a GABA receptor would, but is only an analog. It's not regulated, metabolized or otherwise converted into something that is used. As a result, it has very few side effects and can be a good choice for dogs with kidney and/or liver concerns. It may be associated with some temporary sedation and in humans has been known to very rarely cause huge behavioral shifts, so clients should be aware of a potential for profound 'personality changes', although they have not yet been reported.

**** Important point:** Some benzodiazepines prescribed for pets can cause or aid abuse or addiction problems in humans. Know your household and your visitors, and minimize risks.

b. Tricyclic antidepressants and related compounds:

(TCAs) work by inhibiting the amount of ***norepinephrine*** - a stimulating neurochemical - and ***serotonin*** - a neurochemical associated with calm, outgoing, happy behaviors - that is recycled by the neuron that first releases it (the pre-synaptic neuron). In other words, TCAs block the neuron's own recycling system.

The brain is a truly unique organ and not a lot of chemicals that are in the blood actually get into the brain because of something called the blood-brain-barrier (BBB). The BBB's job is to maintain the overall or total brain at relatively constant conditions so only the smallest

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substances can go easily back and forth between the brain and the blood. This is one reason why recycling of neurochemicals is so important: this is a conservation strategy for neurochemical building blocks.

Because neurochemicals work by stimulating receptors in the next neuron (the post-synaptic neuron), the extra neurochemicals hanging around the space between the neurons (the synaptic cleft) are now available to stimulate the next receptor that becomes available. This means that you do not have to stimulate the first cell (the pre-synaptic neuron) again, to continue to stimulate the second cell. This pattern is so powerful that it overcomes the thermostatic effect experienced by the first cell. Now that you have all this neurotransmitter hanging around, the cell's thermostat (otherwise called the somatodendritic auto-receptor) tells the first cell not to move any more neurochemical to the cell's membrane because there is already more outside than is being used. Accordingly, the first cell slows down its production and movement of norepinephrine and serotonin. Since the entire point is to stimulate the receptors in the second cell so that they stimulate chemicals in the cell that affect overall activity, it's more important to have stuff available to fill the receptors than it is to have continuous supply. After a few days, a new set-point or thermostatic level is reached and there is both high volume of neurotransmitters moved through the pre-synaptic neuron and efficient saturation of receptors on the second cell (the post-synaptic neuron).

c. Selective serotonin reuptake inhibitors and related compounds:

SSRIs work very much like TCAs do, but they have very, very small or virtually no effects on norepinephrine. The different SSRIs (eg, fluoxetine (Prozac in the USA), paroxetine (Paxil in the USA), sertraline (Zoloft in the USA), et cetera) affect different types of different serotonin receptors to a greater or lesser extent, which is why sometimes a few tries are needed before choosing the best medication for your pet. Just like people, dogs and cats differ in receptor density, in receptor type distribution, in overall metabolism of the medication, and in which enzymes make them more or less sensitive to a drug. Unfortunately, the only way to learn or infer this is to try different medications if another is not working. Because of their more selective effects on receptor types, SSRIs are usually considered to have fewer side effects than many other medications, which is why they are used so often.

SSRIs and the more specific and newer of the TCAs (eg, clomipramine / Clomicalm®) do their best work by changing the metabolism of the second neuron and encouraging it to stimulate its genetic and protein making machinery to make new and better receptors. This is also the process you go through when learning something new. ***Because of this pattern, treatment with the appropriate TCA and, or SSRI can help your pets learn the behavior modification faster than they would without the medications.***

In placebo controlled, double blind studies, dogs treated with TCAs and SSRIs plus behavior modification compared with those treated with behavior modification, alone, improved faster and to a better level. This one of the reasons these medications are so often used in treatment

programs.

**** Important point:** SSRIs and some TCAs are recommended because they help dogs learn. They do this by decreasing the anxiety that interferes with learning and by using the neurochemical pathways that are already involved in learning.

d. Combination SSRIs/ TCAs:

Some of the newer medications (eg, Effexor; venlafaxine) are medications that have the beneficial effects of the TCAs and SSRIs, combined, which minimizes side effects. This means that they will stimulate both the more specific and less specific neurochemical receptors, and will effect both norepinephrine and serotonin, but at different rates than would the SSRI or TCA, alone. Because of these changes, some of these medications can have fewer side effects and greater treatment effects for some patients. All of these compounds still have their patents at this writing which can make them a little pricier than some of the other, 'older' medications. The same effect may be achievable by combining the TCA and the SSRI in the animal, using 2 different medications, at relatively lower dosages.

e. Memantine and related compounds:

Glutamate is an excitatory amino acid. It stimulates other neurons using various receptors. Increases in glutamate have been reported in a number of cognitive, epileptic and behavioral conditions that involve explosive or impulsive behaviors. Memantine blocks the binding of glutamate with a specific receptor class and so decreases the adverse effects of glutamate.

f. Clonidine and related compounds:

Clonidine is a member of the class of medications known as centrally acting, alpha-2 agonists. These medications decrease cardiac output and lower blood pressure, and so should beneficially affect the increased heart rate, tone and arousal that are reactions to stress, threats or excitement. By blocking the action of these receptors, medications like clonidine are thought to act by preventing the physiological effects of arousal in upsetting situations (e.g., storms, loud noises, novel situations that cause panic). Such medications should be used with care if there is any heart disease, or if they are used with medications that increase norepinephrine (adrenalin).

g. Monoamine oxidase inhibitors (MAO-Is):

MAO-Is are not widely used in veterinary behavioral medicine but one MAO-I is licensed for use in the USA to treat cognitive dysfunction in dogs: selegiline (Anipryl). MAO-Is work in the same way as TCAs and SSRIs, except that their focus is on the neurochemical, dopamine. Dopamine receptors are common in parts of the brain affected by aging and increasing dopamine may help those experiencing age-related behavioral changes in cognition. Dopamine is metabolized to a version of amphetamine, so some of the desired behavioral changes we see in elderly dogs and cats treated with selegiline may be due to being more active. Dopamine is a neurochemical in its own right, but it is also a precursor for norepinephrine (adrenalin), so we cannot combine TCAs or SSRIs and MAO-Is because we may cause a huge pulse of adrenalin

and/or serotonin.

6. Combination treatment:

BZD can be used in combination with TCAs and SSRIs, when called for. For example, many dogs with separation anxiety are also afraid of storms. Storms may not happen every day, so we won't want to give a medication daily that the dog may not need. The dog can take a TCA like clomipramine (Clomicalm®) every day, and the BZD, alprazolam, as needed. This means that for 20 days of a month the dog may get the TCA twice a day, but for 10 days she also gets the alprazolam as needed if there is a 50% chance or greater of storms. Because dogs use up alprazolam quickly and have few really sedative effects of repeat dosing if the dose chosen is correct, the dog may get alprazolam 3 or 4 times a day during those 10 days of storms.

There is currently no ideal drug to control or treat both of the chronic and sporadic types of anxieties. The best way to do this is to use the 2 different drugs in a rational way. This means your veterinarian needs to understand how they interact for effect and for side effects. For example, a dog whose only problem is storm phobia may need a higher dose of the alprazolam than a dog who also has separation anxiety and is already taking a TCA or SSRI. The choice has to do with the threshold that makes the dog react and how quickly the individual dog metabolizes the medications. Like humans, dogs and cats can either be slow or fast metabolizers. We know very little about this, currently.

Another kind of combination treatment is often used for the treatment of canine anxieties. As mentioned briefly above, this involves using a combination of TCAs and SSRIs (e.g., amitriptyline and fluoxetine), together. There are 3 reasons for doing this:

(1) If cost is an issue, by using a less specific medication with a more specific one, the amount of the more specific - and generally costlier - drug will be decreased.

(2) Sometimes some amount of the less specific drug is needed to affect receptors more specific drugs don't. Although the problem is mainly with the receptors the more specific drug addresses, clinical experience indicates that the behaviors differ when either medication is given, but both have desired improvements. In this case, using lower dosages of both drugs, especially if they are TCAs and SSRIs, can facilitate each other - or make each drug work better. This is especially true for drugs that share mechanisms for how they work.

(3) By using lower dosages of 2 drugs the side effects of each drug may be minimized.

However....caution is urged at the beginning of the combination treatment. The very, very rare animal shows an exaggerated excitation response which may be *equivalent to serotonin syndrome in humans*. These animals are quickly recognized because they don't stop moving, don't sleep, don't eat, and are generally frantic. *Medications should be stopped at once for any animal exhibiting these signs and the veterinarian should be informed immediately.* Treated

appropriately, dogs and cats survive these episodes, but may never be able to take the same amounts or types of drugs again. To repeat, this is a very, very rare side effect, but in the world of side effects, knowledge is power.

**** Important point:** You **cannot** give TCAs or SSRIs along with an MAO-I (monoamine oxidase inhibitor; e.g., Amitraz®, Preventics®, Anipryl®) because both increase the amount of norepinephrine (adrenalin) available, and the combination may also increase the amount of serotonin available, increasing the risk of serotonin syndrome!

7. The medical aspects of treatment with behavioral medications:

Almost all medications used in the treatment of behavioral problems are metabolized or broken down and excreted by the liver and kidneys. Because of this, and because of the rare, but potential concerns about effects on heart function, every animal treated with any behavioral medication should have both a thorough physical examination, including at least a good listen to their heart, and a complete blood count, urinalysis, and serum biochemistry profile - just like you have when you have your annual physical - to make sure that nothing is wrong with their liver, kidney, or other organ systems, *and* that the behavioral concerns are not non-specific signs of a physical condition.

Most behavioral signs are non-specific and may be the result of a physiological condition. A good history will usually help clarify the diagnosis, but a good physical examination is essential. If your veterinarian has concerns he or she may want to also do some radiographs and, or an electrocardiogram, but the need for such follow-up is not common.

If your pet has some liver or kidney compromise, you may still be able to give them behavioral medications but you may need to use a lower dosage or give the medications less frequently.

If your pet is treated with behavioral medications long-term - and many pets need this - you should have the physical and laboratory exams repeated at least annually, or if the pet becomes ill. As pets age, their ability to process medication may change. Again, by changing dose or frequency these changes can usually be well managed, but you need to know the change has occurred. The only way to do this is to have a laboratory evaluation, and for some older dogs and cats this should be done 2-4 times a year. Remember, your pets cannot tell you when they are beginning to feel a little odd.

There are some medications that interact with the behavioral medications that you pet is taking. The common conditions that require treatment with medications that may interact with behavioral drugs include epilepsy, hypothyroidism, and, especially in cats, diabetes. Having these conditions does not mean your pet cannot be treated with behavioral drugs, but it does mean that treatment should be thoughtful. For example, treatment with a TCA can alter the level of the thyroidal hormones that are measured on routine tests. In some cases, lower doses of drugs used to treat epilepsy may be needed if the dog is calmer. However, the combination of

required drugs may make some animals sluggish. Every animal is an individual and your job as your pet's best friend is to ask questions that will allow you to look out for your pet's best interests.

**** Important point:** Medical conditions can affect how well your pet can utilize behavioral medications. Additionally, behavioral drugs can interfere with the metabolism of medications used for other conditions, and those medications can interfere with the ability of your pet to respond to behavioral medications. You need to discuss all of this with your veterinarian as your dog or cat ages or requires other help.

8. Length of treatment required:

The amount of time that your animal takes behavioral medication will depend on the following 4 factors:

- how long the pet was affected before beginning treatment or how early in the course of the condition the pet is treated. The longer the pet was affected, the more numerous are the neurochemical changes in the brain associated with learning the anxiety. If pets are treated early in the course of their condition, treatment is likely to be relatively short (e.g., 4 or 6 months rather than life-long).
- how severely the pet is affected (e.g., does your dog exhibit all of the signs of separation anxiety or a just a few of the milder ones?). The more severely affected the pet is, the more likely are pathological changes in brain neurochemistry in affected regions. Also, the more profound the fear, the more quickly it's learned and honed by practice. Severely affected pets may have a lesser probability of weaning from a medication than do mildly affected pets.
- how well you can comply with the other aspects of the treatment: The harder people work with behavioral and environmental modification, the more likely the pet is to become well, and less they may need medication. Because medication speeds the rate at which dogs acquire the behaviors encouraged by behavior modification, there is a synergy between effort and medication so that people who work the best and hardest have a greater likelihood of being able to wean their pets from medication.
- your tolerance for giving behavioral medication to your pet: People who are frantic about potential side effects hover over their pets and make their anxieties worse. Although this isn't what they intend to do, some people are just so uncomfortable with using behavioral medication that it may not be the best - or at least the first - choice for them.

In general, the average dog or cat treated with daily medication will require treatment for 4-6 months before any weaning should be attempted. This not only allows for improvement to occur but allows you and your veterinarian to gauge how reliable that improvement is as life varies. Please keep a list comparable to that kept by your veterinarian of the pet's weight, medication given, frequency given, amount given and any changes. You will also want to note dates when medication has been refilled. By keeping this list accessible (put it on the refrigerator) you will guarantee that your pet is getting the appropriate medication, as agreed

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with your veterinarian. A sample table is attached.

Like humans, some dogs and cats will require lifelong medication, some will require sporadic medication, and some will require just one round of medication. Unfortunately, we do not know enough to predict in advance which dog or cat will require what. Think of these conditions like diabetes.....some forms of diabetes require only lifestyle changes, some require initial treatment with insulin while implementing lifestyle changes, and some require insulin no matter what. Some dogs have neurochemical receptors that can re-regulate on their own, some will need medication forever to insure that this happens.

Regardless of how long your pet requires medication, by following the recommendations in this protocol you can assure that you are giving the medication safely and in the pet's best interests.

When stopping medication, weaning is preferred over an abrupt halt. This is because:

- abrupt halts can trigger relapses,
- by weaning you have earlier warning that the changes are going in the wrong direction,
- by weaning you can learn if your pet still needs medication, but at a lower dose, and
- clients are less worried when changes are gradual.

Some clients never wish to wean their pets from medication because they are afraid that their animals will suffer. Our incomplete ability to assess our companions' suffering is one of the real difficulties of loving dogs and cats who cannot speak. Treatment for behavioral conditions should - first and foremost - be humane and in the best interests of the pet. That said, if clients are not sure that they can tell if the animal begins to suffer or relapse, and they are worried that their pet will worsen if weaned from medication, there is nothing wrong with continuing medication as part of a treatment program involving behavior modification and environmental intervention, as long as potential physical concerns are addressed, as discussed above.

**** Important point:** Discontinuation of medication abruptly is **not** recommended because of the risk of relapse and because of the potential for 'dyscontinuation/withdrawal syndrome'. That said, all of these medications can be stopped quickly if needed in an emergency, and none are addictive.

9. Other concerns:

Pets treated with behavioral medication can otherwise be treated as we do non-treated dogs and cats. Anesthesia poses special concerns, but these are easily addressed by your veterinarian by considering how the drugs your pet is taking could interact with other medications. Because of the risk of relapse and because anxiety is not helpful during anesthetic procedures, the general recommendation is to maintain the dog or cat on his or her anti-anxiety medications and alter the mix of drugs given as part of the anesthesia cocktail. If your veterinarian is not comfortable with this idea, please suggest that they speak to a specialist. The field of veterinary behavioral medicine is still relatively young, and most vets do not receive any training in behavioral

From: Overall KL. Clinical Behavioral Medicine for Small Animals, Mosby, St. Louis, 1997 and Overall KL. Manual of Clinical Behavioral Medicine for Dogs and Cats, Elsevier, St. Louis, 2013.

medicine while they are in vet school.

10. Transdermal patches and gels:

Clients and veterinarians, alike, would welcome a topical gel or patch for these medications. Unfortunately, the metabolism of these medications changes dramatically when absorption through the skin taken is compared with taking the medication by mouth. In the few studies that have been done, a much larger amount of medication is needed for the same effect - if the medication is applied to the skin. Thus far, this finding has made patches and gels impractical for behavioral treatment. Future treatments may be more flexible.

11. Last words:

Please remember - drugs are part of a treatment plan that involves changes in the environment and behavior mod.....***do not think that drugs, alone, will accomplish what an entire treatment plan can.*** And, unfortunately, like the rest of life, there are no 'quick fixes'.

Please do not seek to mask normal behaviors by sedating your pet. This is an inappropriate use of medication, and most of the medications discussed here will not do that anyway.

Finally, please remember safety. Any drug can be toxic if huge quantities are ingested. Dogs, puppies, and kittens often chew on pill containers. This is the most common reason for 'overdose' in pets. While the container, itself, is likely to do more damage to the animal if broken and eaten, support for these animals can require a lengthy stay in an intensive care unit. No one wants to sustain the financial or emotional costs for that. So.....be a good guardian. Put medications far away from the curious hands of children and paws and mouths of puppies and kittens. Unless you have difficulty opening pill bottles, request safety lids. Safety lids are harder for dogs to open, too, but not to chew through. Common sense may not be common, but it works. In the USA, the ASPCA's poison control center can be reached at: <http://www.aspc.org/Pet-care/poison-control.aspx>; 1.888.426.4435.

**** Important point:** Drugs, behavioral medications, psychotropic medications, whatever you wish to call them - **are not a quick fix.** You cannot just give a pill and expect years of anxiety to vanish. But used rationally and safely, behavioral medications actually allow you to help your pet and to become more humane in doing so.

Summary of commonly asked client questions with answers:

Client question	Quick answer
What medications are used?	We use most of the same medications or classes of medication that are used for the same conditions in humans. Most commonly used medications come from the BZD, TCA and SSRI classes of drugs.
How do these work?	All of these medications affect how brain neurons communicate with each other and the neurochemistry that appears impaired in anxiety.
What are the potential side effects?	Side effects are usually rare and transient but can include GI distress including diarrhea and/or regurgitation/vomiting, changes in appetite including anorexia, sedation, changes in energy level, atypical reactivity, and increased heart and respiratory rates. If any of these side effects are profound or last longer than a few days, the patient should be re-evaluated. Anorexia is a rare but profound problem for some patients given SSRIs. Serotonin syndrome is a concern for any patient taking any medication that affects serotonin and who is experiencing profound increases in heart rate, body temperature, and/or agitation.
How should the client monitor for side effects?	<p>Clients should keep a log of the worrisome behaviors, and compare them to normal. To do this, they need to know if the dog or cat occasionally has diarrhea and what their behaviors were before starting medications.</p> <p>Clients can learn to take patients' heart rates and report any significant increases or decreases immediately to their veterinarian.</p> <p>Client can also comply with the recommendation for annual physical and laboratory evaluation for younger animals and twice annual evaluation for older animals. Evaluation should also occur if the dog or cat becomes ill.</p>

<p>Can these medication interact with other medications (e.g., thyroxin, anti-inflammatories, pain medications like tramadol) and, if so, how?</p>	<p>Yes, any medications that use the same enzyme system in the liver can have their effect exaggerated or decreased, depending on the enzyme function, and those medications can have the same effect on the behavioral drugs. This is why it is so important for clients to ensure that they tell their veterinarian every single medication and supplement that their dog or cat is being given. Clients need to understand that this list includes ‘homeopathic’, ‘herbal’, and ‘natural’ products. St. John’s wort, for example, is a potent CYP 3A4 inducer.</p> <p>For medications like thyroxin, there may be effects on measured blood levels of the medication or on the compounds it is intended to affect.</p> <p>Pain medications (e.g., tramadol), antibiotics and anti-inflammatories can be given with behavioral medications if they are needed, if the dosages are appropriately adjusted and the patient monitored, which is easy to do. Anti-inflammatories may block some effects of SSRIs but there are no data yet for dogs and cats.</p>
<p>I know that I cannot use a Preventics® collar (which contains amitraz) or other productions containing amitraz for my dog if he/she is taking TCAs or SSRIs. Can I use topicals (Frontline®, Advantix®, pyrethrin sprays, et cetera)?</p>	<p>Amitraz is an MAO-I which can produce a toxic response when given to a patient already taking an SSRI or a TCA. Any product containing an MAO-I should be avoided if the patient is taking a TCA or an SSRI.</p> <p>Frontline® (fipronil) and Advantix® (imidacloprid, permethrin and pyriproxyfen) do not use MAO-Is and instead rely on insect growth hormone inhibitors. Advantix® also has a pyrethrin (permethrin) which acts as repellent and neurotoxin for insects. These medication can be used with TCAs or SSRIs.</p> <p>However, if the patient is a cat.....you must</p>

	avoid pyrethrins. They are toxic for cats.
What effects can be seen and when?	<p>Dogs and cats treated with medications affecting anxiety should become calmer and less anxious.</p> <ul style="list-style-type: none"> • This may mean a decrease in activity which can appear as weight gain. • Patients may actually eat more, and may finish their food treats/food toys when the clients are not with them. Contrast this with anxious patients who cannot eat when distressed and who will not eat or finish treats or food toys when alone. • Patients who are less anxious may react less quickly to a stimulus. • Less anxiety patients may react to a certain stimulus using a lower level of reactivity level than was previously possible. • Less anxious patients may raise their threshold for reacting and so not react as readily as they had previously. Now, it takes more of a stimulus to make them react. • Patients who are improving may show a decreased amount of time between hearing the request to lie down or sit down and compliance with the request. They are less worried and so can comply more readily. • Patients who are deriving beneficial effects from their medication may pause before reacting or become more thoughtful and less concerned, in general. They may be able to attend more to cues in the environment and assess whether they need to react before reacting. • Patients may sleep longer and more soundly (more restorative sleep) as their anxiety resolves. • Patients may be more receptive to

	<p>learning to change their behavior through behavior modification.</p> <ul style="list-style-type: none"> • Patients may become more attentive to the helpful cues they are given, and they may solicit cues more often. • Dogs who are improving may take treats more gently rather than grabbing forcefully at them as concerned dogs often do. Here, it is important to separate poor delivery technique from patient anxiety. • Cats who improving may become more interested in behavioral modification using food treats, and be willing to remain with the client to learn about these.
<p>How long must the patient take the medication?</p>	<p>Patients affected for a long time may require or benefit from long-term treatment. Patients with relatively uncomplicated, recent concerns may require medication for only a few months. Length of treatment is determined by the patient's history, the patient's treatment response, the client's concerns, and the patient's stimulatory environment.</p>
<p>How do we wean or remove the patient from the medication?</p>	<p>If there is an emergency patients can be abruptly taken from the medication, but weaning is preferred in planned cessations. Weaning permits the avoidance of rebound syndrome and allows clients to learn if their pet would benefit from a lower dose of the medication. Be aware that some patients who are removed from a medication will not respond to it when exposed again, no matter how well they did when treated with it the first time.</p>
<p>What does the client do if he or she is scared?</p>	<p>The client should call their vet immediately and express the details of the concern to a member of the treatment team. If the concern is after hours and no one returns a phone call quickly, the client should take the dog or cat to any emergency service to err on the safe side and to prevent the possibility of feeling guilt.</p>

