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# BEHAVIORAL PHARMACOLOGY IN SHELTER SETTINGS

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Maddie's Fund/ Association of Shelter Veterinarians

## Outline

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- **When to prescribe**
- Monitoring
- Medication choices
- Outcome considerations

## Medications for Shelter/ Rescue Dogs

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- Address immediate welfare concern
  - Improve adoptability
  - Smoother transition to new home
  - Shorter term treatment
- Address behavior disorder
  - Improve welfare short and long term
  - Make less adoptable pet more adoptable
  - Able to maintain pet in a home long term

## Guidelines for Use

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- Goals of medication use
  - Address specific underlying neurotransmitter alterations
  - Decrease reactivity
  - Make behavioral and environmental modification easier to implement
  - Medications do not change pet's behavior itself
    - Modify **underlying emotional state** contributing to problem

Overall 2004
Luescher 2009

## When to Prescribe

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- Things to consider
  - Risk assessment
  - Shelter's resources
  - Shelter's community

## When to Prescribe

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- Risk Assessment
  - Safety- animals and people
    - Physical and emotional risk
  - Quality of life assessment
    - Be improved to life worth living or enjoyed?
    - Pet and person
    - Re-evaluated at regular intervals
  - Risk of continued behavioral deterioration
    - What is the risk of waiting?
    - Problem worsen to become dangerous or the welfare so severely compromised cannot recover?
    - Unacceptable to keep pet in current situation where improvement cannot be made and deterioration is inevitable

## When to Prescribe

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- Shelter's Resources
  - Can your organization manage this behavior problem?
    - Manpower
    - Time
    - Education

## When to Prescribe

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- Shelter's Community
  - Community willing to take on this problem in a pet?
    - Asilomar classification?
  - Community's perception on behavior medication in general

## When to Prescribe

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- Requirements to Prescribe
  - VCPR
  - Medical evaluation
  - Diagnosis or working diagnosis
  - Always consider other treatments that can be implemented
  - Lab work?
  - Follow up plan

## Outcome Options/ Other Treatments

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- "Plan for the worst, hope for the best."
  - Best to have back up plan
  - Recommend ideal plan first, if declined, give 2nd option
- Remember potential consequences for no option B for shelter pet
  - Is it fair for the options to be adopt or die?

# Outline

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- When to prescribe
- **Monitoring**
- Medication choices
- Outcome considerations

# Monitoring

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- Designated person
  - DVM there daily? Technician? Experienced handler/ caregiver?
- Daily rounds being performed?
  - Monitor appetite, water intake
  - Urination, defecation
  - Level of activity
  - Level of undesired behavior
  - Level of anxiety/ stress related behaviors

# Monitoring

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- Follow up plan
  - Within organization
    - When do you want to hear back?
    - Who to contact? How?
      - Do they know when to contact you?
    - Side effects
  - Reassess plan and adjust
- Plan to go with pet- outcome

# Outline

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- When to prescribe
- Monitoring
- **Medication choices**
  - **Brief review of neurotransmitters**
- Outcome considerations

# Neurotransmitters

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- Chemical messengers
  - Glutamate
  - γ (gamma) aminobutyric acid (GABA)
  - Acetylcholine (Ach)
  - Monoamines
    - Dopamine (DA)
    - Norepinephrine (NE)
    - Serotonin (5-HT)


# Glutamate

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- Amino acid
- Major excitatory neurotransmitter in brain
- Est. 60- 75 % of brain uses glutamate (Crowell-Davis, Murray 2006)
- Abnormal levels in impulsive, aggressive, and schizophrenic disorders in people (Overall 2001)

# GABA

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- GABA- γ (gamma) aminobutyric acid
- Synthesized from glutamate
- Major inhibitory neutrotransmitter in CNS
- Role in vigilance, anxiety, muscle tension, seizure activity, and memory (Crowell-Davis, Murray 2006)

# Acetylcholine (Ach)

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- Synthesized from choline and acetyl coenzyme A (acetyl CoA)
  - Only neurotransmitter not directly synthesized from an amino acid
- Postganglionic parasympathetic synapses (muscarinic), autonomic ganglia/ brain/ adrenal medulla (Nicotinic n), and neuromuscular junctions (Nicotinic m)
  - Involve learning and memory
  - Reward and dependence systems activated

# Neurotransmitters

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- Monoamines (biogenic amines)
  - Catecholamines:
    - Dopamine
    - Norepinephrine (noradrenaline)
    - Epinephrine (adrenaline)
  - Indolamines
    - Serotonin
    - Melatonin
  - Histamine

# Catecholamines

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- Tyrosine → Dopa → **Dopamine** → **Norepinephrine**
  - DA and NE cell specific
- DA- phenothiazines, MAOIs, natural rewards
  - Substantia nigra
- NE- alpha and beta adrenergic
  - Agonist/antagonist activity at pre- or post-synaptic receptors
  - Locus coeruleus

# Serotonin

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- Tryptophan → 5-hydroxytryptophan (5-HTP) → 5-hydroxytryptamine (5-HT, serotonin) → melatonin
- Midbrain raphe
- 14 + receptor types
  - Involved in medication side effects

# Serotonin

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| RECEPTOR | FUNCTIONS |
|---|---|
| 5-HT 1A | Prereceptor: autoreceptor- inhibits firing of neuron, synthesis, and release of 5-HT; postreceptor |
| 5-HT 1B | Autoreceptor- inhibits additional 5HT release |
| 5-HT 2A | Platelet aggregation and smooth muscle contraction |
| 5-HT 2B | Found on human heart valves |
| 5-HT 2C | Regulates appetite |
| 5-HT 3 | In GIT, CRTZ (vomiting, nausea) |
| 5-HT 4 | GIT (secretion and peristalsis) |
| 5-HT 6 | Limbic system |
| 5-HT 7 | Limbic system |

# Medication Choices

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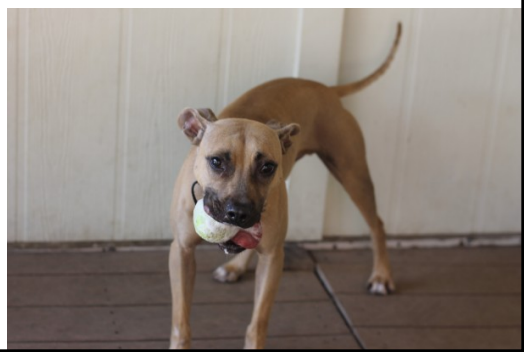
- What is your goal?
  - Kennel stress, immediate welfare control
    - Short onset medication
      - Benzodiazepines
      - Trazodone
      - Clonidine
      - Gabapentin



# Medication Choices

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- What is your goal?
  - Anticipate long term management of behavior disorder
  - Pet with anticipated long term stay
    - Longer term chronic daily dosing might be appropriate
      - Separation anxiety
      - Generalized anxiety
      - Significant/ frequent fears
      - Compulsive disorders
    - SSRIs
    - TCAs
    - Azapirones

# Medication Choices

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- Administration requirements
- Frequency
  - Does the organization have the manpower to medicate multiple times per day?
  - Lower frequency, better compliance
- Route- Most are oral
  - Mix in food, pill pockets, peanut butter, etc.
- Difficulty administering
  - Aggressive, fearful animals
    - Level of stress of administration worth the benefit of medication?
      - Cats

# Medication Choices

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- Cost, availability
  - Money and time most often limiting factors
    - Not for profit
    - Rely on donations, grants
- Abuse potential
  - If you are not there to monitor, manage, who is?
  - Staff, volunteer diversion risk

# Medication Choices

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- Legal constraints
  - Rabies observation
    - Behavioral side effects mimic neurologic changes?
  - Court ordered holds
    - Requirement to hold “evidence” in manner to prevent deterioration
      - Physical health but also mental health
    - Long term holds
      - Welfare concerns
  - Discuss concerns with officers involved

# Back to the Medications…

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- Fast acting Short term medications

# Medication Choices- Dogs

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| Drug Class | Drug Name | Dose | Side Effects | Schedule |
|---|---|---|---|---|
| Benzodiazepine (GABA) | Clonazepam (Klonopin ®) | 0.1-1 mg/kg | Sedation, hypotension at high doses | PO PRN or q 8-12 hrs |
| Benzodiazepine (GABA) | Alprazolam (Xanax ®) | 0.01-0.1 mg/kg | Paradoxical excitation | PO PRN or q 8-12 hrs |
| Serotonin Antagonist and Reuptake Inhibitor (SARI) | Trazodone (Desyrel ®) | 2-10 mg/kg Maximum 300 mg per dose | Sedation, GIT side effects especially with initial doses | PO PRN or q 8-12 hrs |

Fast acting- immediate stress and anxiety control

# Medication Choices- Dogs

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| Drug Class | Drug Name | Dose | Side Effects | Schedule |
|---|---|---|---|---|
| $\alpha_2$ Adrenergic Agonist | Clonidine | 0.01-0.05 mg/kg | Sedation, hypotension at high doses | PO PRN or q 6-8 hrs |
| Anticonvulsant/ Neuropathic analgesic | Gabapentin (Neurontin ®) * Not liquid | 10-30 mg/kg | Sedation, ataxia | PO PRN or q 8-12 hrs |
| Phenothiazine (Dopamine, others) | Acepromazine | 0.1-2.2 mg/kg | Tranquilizer, not an anti-anxiety agent | PO PRN |

Fast acting- immediate stress and anxiety control

# Medication Choices- Dogs

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- Medications
  - Phenothiazine
    - Acepromazine
      - Tranquilizer
      - Little to no anxiolytic effect
      - Can increase sensitivity to noise
    - **Inappropriate to use alone to manage noise aversions**

Overall, K. 2013

# Medication Choices- Cats

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| Drug Class | Drug Name | Dose | Side Effects | Schedule |
|---|---|---|---|---|
| Benzodiazepine | Lorazepam (Ativan®) | 0.025 – 0.08 mg/kg OR ¼ to ½ of 0.5 mg tablet (0.125-0.25 mg/ CAT) | Sedation, ataxia, hypotension at high doses | PRN or q 8-24 hrs |
| Benzodiazepine | Alprazolam (Xanax ®) | 0.01-0.1 mg/kg OR 0.125-0.25 mg/ CAT | Paradoxical excitation, behavioral disinhibition | PRN or q 8-24 hrs |

Fast acting- immediate stress and anxiety control

# Medication Choices- Cats

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| Drug Class | Drug Name | Dose | Side Effects | Schedule |
|---|---|---|---|---|
| Anticonvulsant/ Neuropathic analgesic | Gabapentin (Neurontin ®) | 5-20 mg/kg OR 50-100 mg/ CAT to facilitate handling | Sedation, ataxia; Human liquid contains xylitol | PO PRN or q 8-12 hrs (open capsule, mix with canned food) |
| Serotonin Antagonist and Reuptake Inhibitor (SARI) | Trazodone (Desyrel ®) | 12.5-100 mg/ CAT | Sedation, GIT side effects especially with initial doses | PO PRN or q 12 hrs (Min 2+ hrs prior to effect) |

Fast acting- immediate stress and anxiety control

# Medication Choices- Cats

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- Medications
  - Benzodiazepines
    - Diazepam (Valium®)
      - Case reports of fatal idiosyncratic hepatic necrosis after oral dosing
      - Clinical signs occur 5-11 days after beginning oral therapy
      - Anorexia, lethargy, vomiting, increased ALT/AST, hyperbilirubinemia
    - **Recc. baseline liver values prior to starting and repeated ~ 5 days after chronic dosing**

Center et al. JAVMA 1996

## Longer Term Chronic Medications

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- Antidepressants


## Serotonin Syndrome

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- Concentration of serotonin too high, reach toxic levels
  - Nausea, confusion, agitation, muscle rigidity, tremors, salivation, hyperthermia
  - May lead to seizures, coma and death
- Occur when combine MAOI and another antidepressant (usually TCA or SSRI) concurrently
  - Inhibition of NT degradation coupled with reuptake inhibition

# Serotonin Syndrome

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- Occur with other combinations as well
  - Multiple MAOIs
    - Amitraz- Mitaban, Preventic collars, Promeris, Certifect
  - Diets high in tryptophan (5-HT precursor)
  - OTC herbal supplements
    - St. John's Wort (act as MAOI or broad spectrum reuptake inhibitor) (Schwartz 2005)
    - Griffonia seed extract (5-HTP)
  - Other serotoninergic medications
    - Trazodone, tramadol- lower risk

# Medication Choices- Dogs

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| Drug Class | Drug Name | Dose | Side Effects | Schedule |
|---|---|---|---|---|
| Selective Serotonin Reuptake Inhibitor (SSRI) | Fluoxetine (Prozac ®) | 1-2 mg/kg | Sleepiness or irritability, inappetence | PO q 24 hrs |
| Selective Serotonin Reuptake Inhibitor (SSRI) | Sertraline Zoloft ®) | 1-4 mg/kg | Mild GIT side effects | PO q 24 hrs or divided q 12 hrs |

Longer term, more chronic anxiety control

# Medication Choices- Dogs

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| Drug Class | Drug Name | Dose | Side Effects | Schedule |
|---|---|---|---|---|
| Tricyclic Antidepressant (NE, 5-HT, α1, others) | Clomipramine (Clomicalm®) | 2-4 mg/kg q 24h or 1-3 mg/kg q12h | Vomiting (give with food), sleepiness, anticholinergic effects | PO q 12 or 24 hrs (see dose) |
| Azapirone Anxiolytic (5-HT 1A) | Buspirone (Buspar ®) | 0.5-2 mg/kg | Side effects uncommon | PO q 8-12 hrs |

Longer term, more chronic anxiety control

# Antidepressants- TCA's

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- **Table 11.1**

Acute *in vitro* biochemical activity of selected tricyclic antidepressants

| TCA | NE | 5-HT | α-1 | α-2 | H1 | Muscarinic |
|---|---|---|---|---|---|---|
| Amitriptyline | +/- | ++ | +++ | +/- | ++++ | ++++ |
| Clomipramine | + | +++ | ++ | 0 | + | ++ |
| Desipramine | +++ | 0 | + | 0 | 0 | + |
| Doxepin | ++ | + | ++ | 0 | +++ | ++ |
| Imipramine | + | + | ++ | 0 | + | ++ |
| Nortryptyline | ++ | +/- | + | 0 | + | ++ |

*Source:* Potter 1984; Potter et al. 1991; Richelson and Nelson 1984a; Richelson and Pfenning 1984b; Potter et al. 1995.

Crowell-Davis, Murray 2006

# Medication Choices- Cats

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| Drug Class | Drug Name | Dose | Side Effects | Schedule |
|---|---|---|---|---|
| Selective Serotonin Reuptake Inhibitor (SSRI) | Fluoxetine (Prozac ®) | 0.5-1 mg/kg | Sleepiness or irritability, inappetence | PO q 24 hrs |
| Selective Serotonin Reuptake Inhibitor (SSRI) | Paroxetine (Paxil ®) | 0.25-1 mg/kg | Mild GIT side effects | PO q 24 hrs |
| Azapirone Antidepressant | Buspirone (Buspar ®) | 0.5-1 mg/kg OR 2.5-7.5 mg/ CAT | Side effects uncommon; increased assertiveness, friendliness | PO q12-24 hrs |

Longer term, more chronic anxiety control

# Outline

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- When to prescribe
- Monitoring
- Medication choices
- **Outcome considerations**

## Outcome Considerations

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- Community perception (Chicago vs. Boston)
- Organization perception ☹
- DVM counseling (state to state variation)
- DVM follow up
- Organization follow up
- Non-compliance

## Myths About Behavior Medication

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- "It's just going to drug my dog."
  - …sedate my dog…
  - …mask the symptoms…
- "It's going to change his personality."
- "He's going to become addicted."
- "It will decrease his adoptability."

## Outcome Considerations

46

- Post-outcome plan
  - Who does adoption counseling/ advises next group of situation?
    - Requirements might vary from state to state
  - Management/ education plan to go with dog
  - Full disclosure a requirement
  - Give recommendation for who the next group should follow up with
    - Veterinarian, you, qualified training group

## Adoption vs. Transfer

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- Adoption
- New owner educated about medication
  - Goals, how to give, what to watch for, who to follow up with
- Plan for continuation or weaning
  - Importance of compliance
  - Discussion of risk of stopping medication abruptly
- Wean before adoption?

## Adoption vs. Transfer

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- Transfer to another organization
  - Shelter, rescue group, foster
- Organization's philosophy/ policies on behavioral medications
- Plan for continuation or weaning
  - Discussion of risk of stopping medication abruptly
- Wean before transfer?

## Conclusions

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- Several uses for psychopharmaceuticals in shelter medicine
- Consider treatment goals, risk assessment, quality of life, shelter's resources and community before deciding to add behavior medication to treatment/ management plan
- Special consideration for medication use in shelter
  - Cost & availability, frequency & route of dosing, time to effect, abuse potential
- Need a plan for monitoring, follow up, and post-outcome management

# Thank You for Your Time!

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