UPDATE ON ANESTHETIC INDUCTION TECHNIQUES

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OBJECTIVES

- Update on Alfaxalone
  - Clinical use and considerations
- Update on current thinking of other induction agents
- Learn what the pros/cons are for various anesthetic induction agents
- Understand the value of the “co-induction” approach

INDUCTION!

INDUCTION OF ANESTHESIA

- Described as a sleep like state
- Anesthetics act on the brainstem/hypothalamus and basal forebrain to control wakefulness

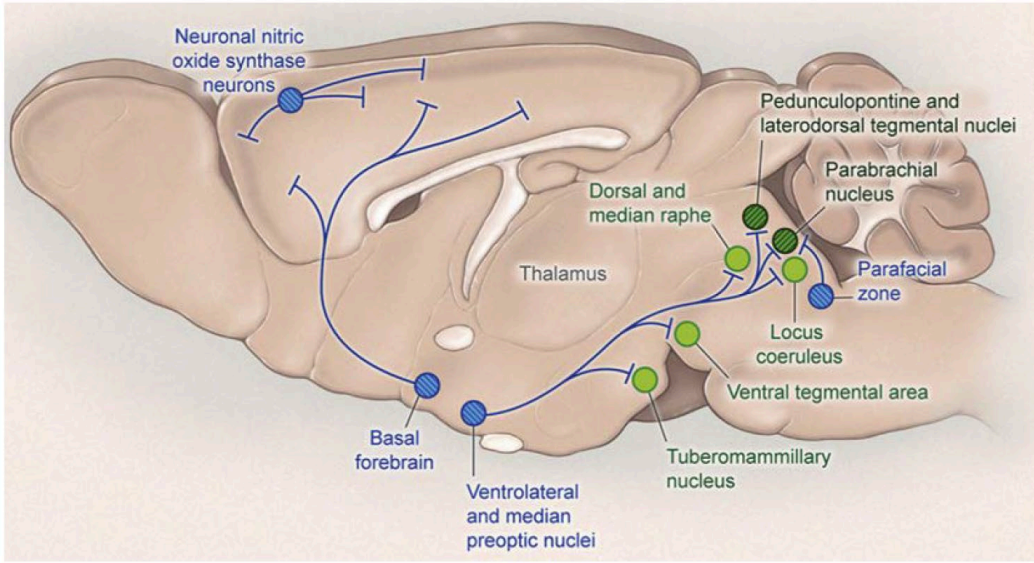


Fig. 9.2 Neurobiology of slow-wave sleep. GABA-ergic neurons in the ventrolateral preoptic area and median preoptic nucleus in the hypothalamus (shown here in rodent brain) promote sleep by inhibiting wake-promoting neurons in the caudal hypothalamus and brainstem. These hypothalamic nuclei are activated by general anesthetics. (Redrawn from Scammell TE, Arrigoni E, Lipton JO. Neural circuitry of wakefulness and sleep. *Neuron.* 2017;93[4]:747–765.)

GOALS OF ANESTHETIC INDUCTION

- Smooth transition from unconsciousness to intubation
- Maintain respiratory drive and breathing
- Minimize risk of regurgitation and aspiration
- Smooth transition from induction to inhalant

PRE-INDUCTION PREPARATION?

- Fast of 4-8 hours depending on meal composition
  - soft vs kibble
- Trazodone 2-10 mg/kg PO at home
- Gabapentin 10 – 50 mg/kg PO at home

- Maropitant 1 mg/kg SQ or PO or IV
  - Helps with PONV

INDUCTION/GENERAL ANESTHESIA

- Balanced anesthesia includes
- Loss of consciousness
- Muscle relaxation
- Loss of somatic reflex
- Blunted autonomic reflex
- Analgesia? Sometimes…..co-inductions

POPULARITY OF INDUCTION TECHNIQUES

- Propofol
- Ketamine-based with benzodiazepine
- Alfaxalone
- Inhalant-based!

Table 3 Reported use of anesthetic agents for induction of anesthesia in dogs undergoing ovariohysterectomy by 1213 respondents in a survey. Respondents could enter more than one response to this question.

Induction drug(s)	**Number of responses (%)**	**Frequency of use *n* (%)**		
		Always/often	**Sometimes**	**Rarely/never**
Propofol	957 (79)	637 (67.0)	153 (16.0)	167 (17.4)
Ketamine–midazolam	863 (71)	235 (27.2)	82 (10.0)	546 (63.3)
Ketamine–diazepam	852 (70)	150 (18.0)	97 (11.4)	605 (71.0)
Tiletamine–zolazepam	854 (70)	89 (10.4)	54 (6.3)	711 (83.3)
Alfaxalone	857 (71)	81 (10.0)	92 (11.0)	682 (80.0)
Ketamine	833 (69)	61 (7.3)	27 (3.2)	745 (89.4)
Mask/box induction	999 (82)	2 (0.2)	29 (3.0)	955 (96.0)

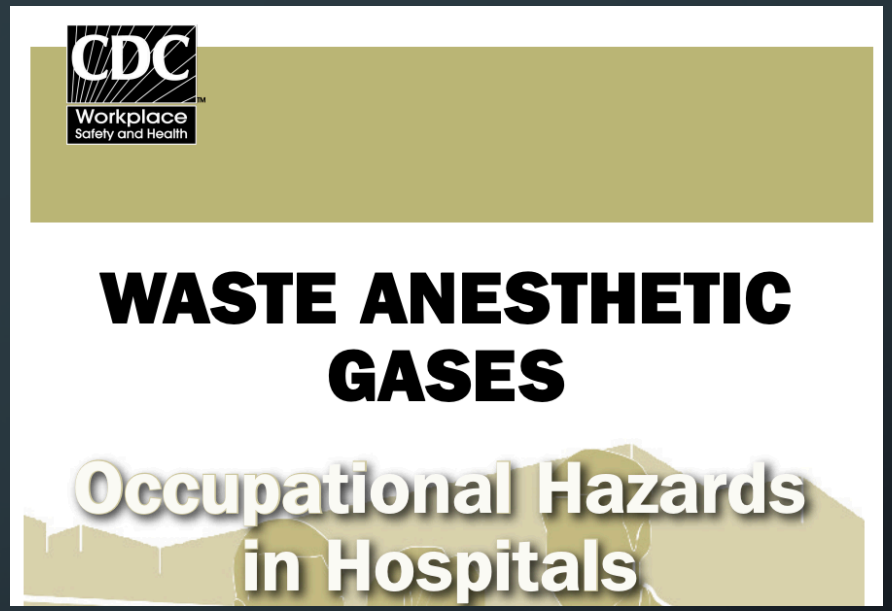
n, number of responses ranking frequency of drug use.

INHALANT INDUCTION

- Controversial method of induction in cats and dogs
  - For so many reasons…..!
- Infrequently used
- Inhalant induction alone led to a 5.9 fold increase in odds of anesthetic related mortality compared to IV anesthetics in dogs

WASTE ANESTHETIC GASES

OSHA
Occupational Safety and Health Administration



- May increase risk of spontaneous abortion
- May increase risk of fetal abnormalities

- Headache
- Irritability
- Fatigue
- Nausea
- Drowsiness
- Difficulties with judgment and coordination


Ames

INJECTABLE ANESTHETICS

- IV is the ideal route of induction in dogs and cats
  - prior to inhalant anesthesia

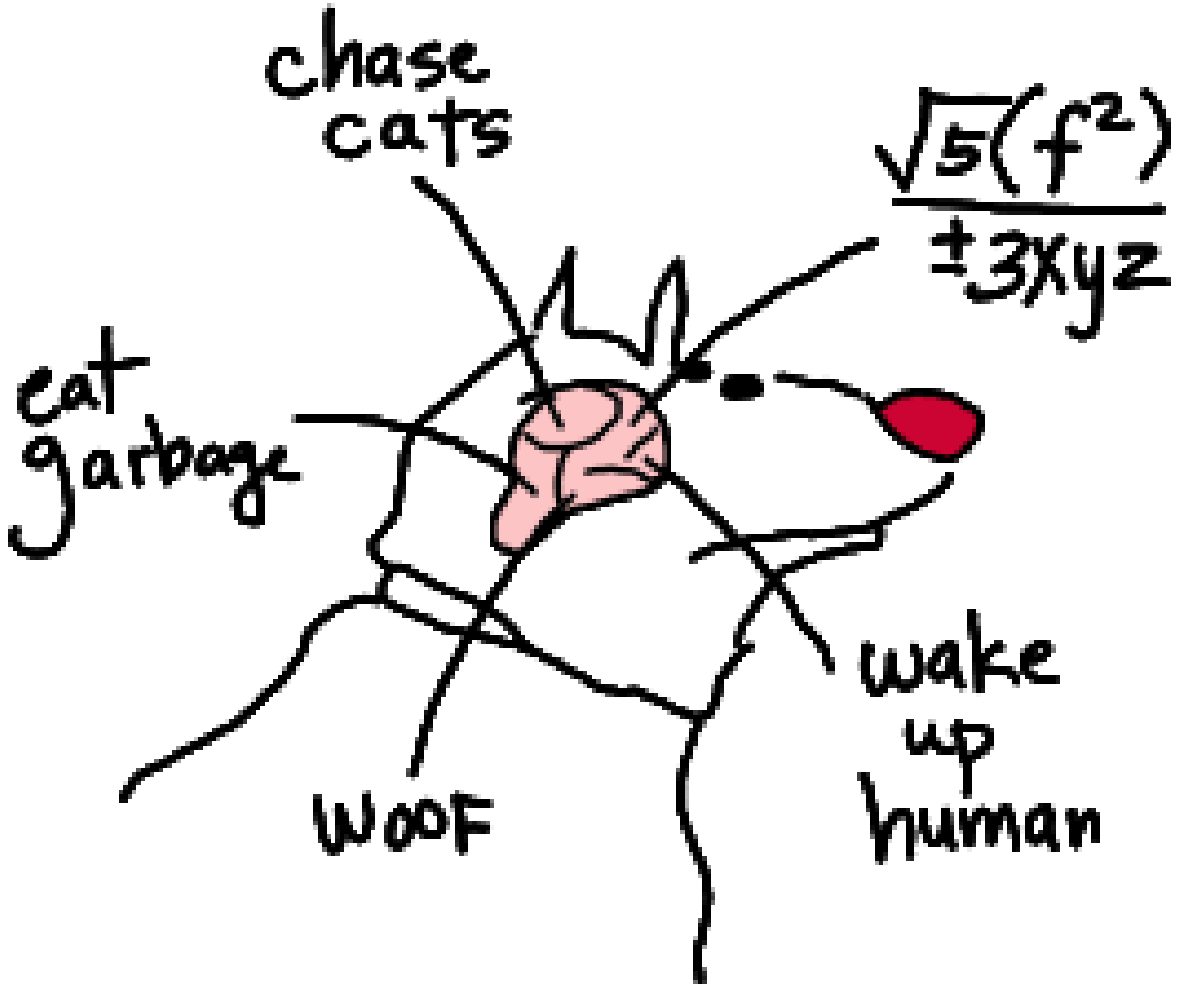
- IM/SQ can be used if IV catheter is unavailable or impractical
- Frequent in general practice for short procedures
- IM/SQ Options
  - Alfaxalone with opioid and sedative!
  - Ketamine with opioid and sedative!

INTRAMUSCULAR INDUCTION TECHNIQUES

- Rarely necessary!
- Patients with difficult IV access?
- Patients with difficult temperament?
- That imposes a huge risk as well!

- Sedative + opioid + anesthetic combination

DOG BRAIN


chase cats
$\frac{\sqrt{5}(f^2)}{\pm 3xyz}$
eat garbage
WOOF
wake up human

AGGRESSIVE DOG PRE-ANESTHETIC ORAL MEDS PLAN

- Trazadone 2-10 mg/kg PO
- Gabapentin 2-100 mg/kg PO
- At Home!

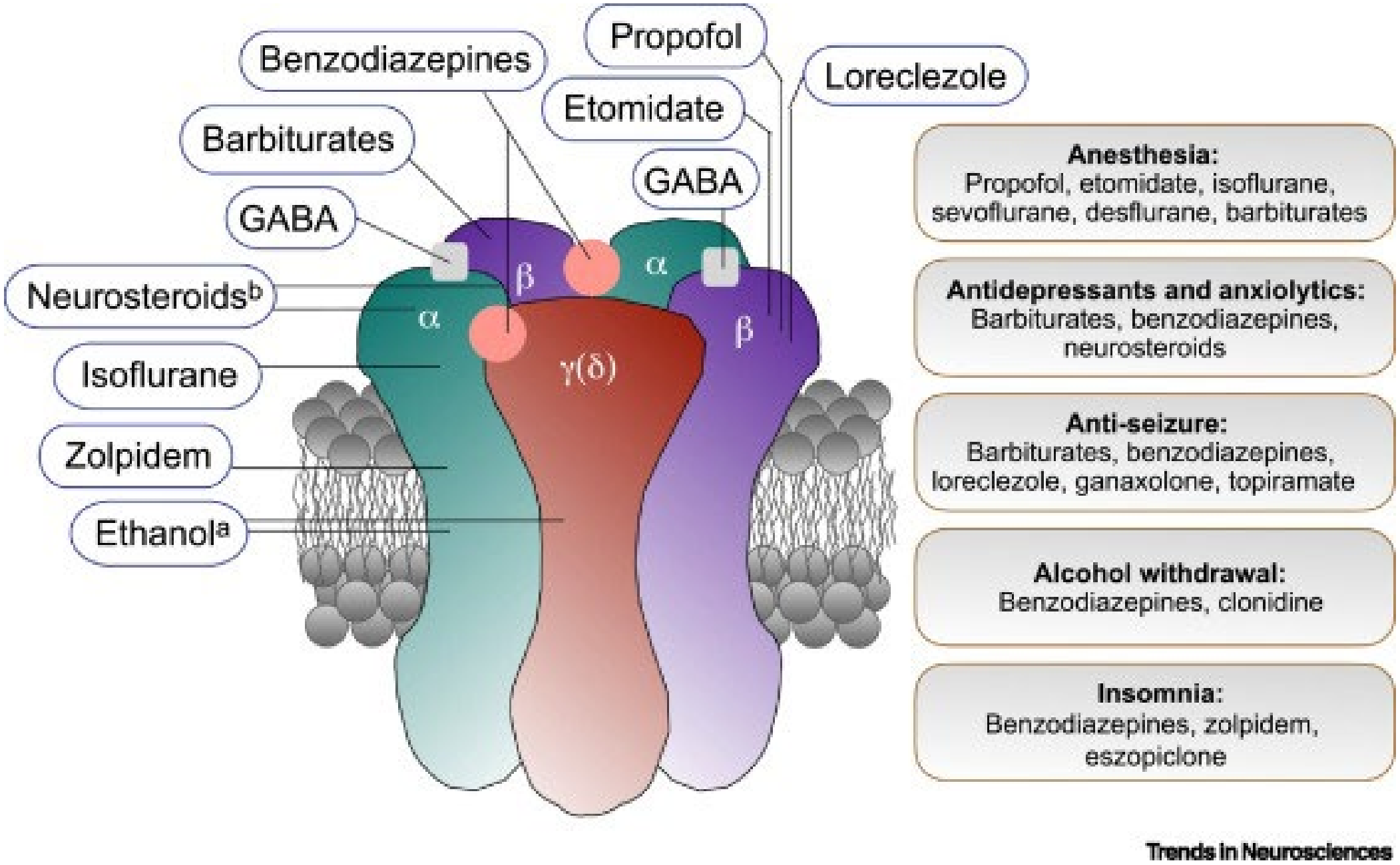
VETERINARY CLINIC PLAN FOR THE AGGRESSIVE DOG

- Premedication with trazodone and gabapentin at home
- “Sileo” transmucosal 10 mcg/kg
- IM dexmedetomidine + opioid of choice

- Basket muzzle
- IV induction drug of choice

INJECTABLE ANESTHETICS

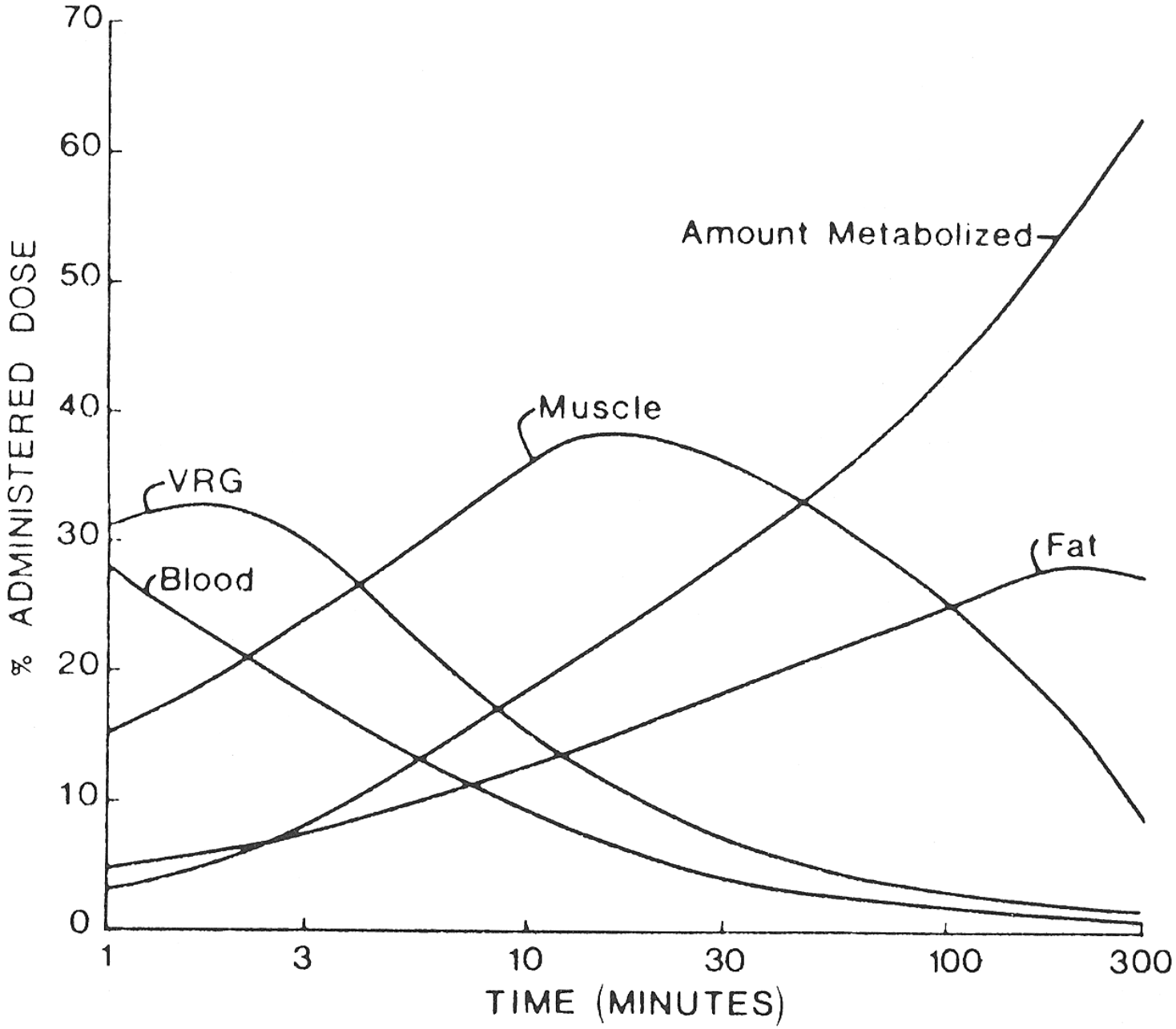
- Propofol
- Alfaxalone
- Etomidate
- Ketamine & Tiletamine



Han W, Shepard RD, Lu W. Regulation of $GABA_A$Rs by Transmembrane Accessory Proteins. Trends Neurosci. 2021 Feb;44(2):152-165. doi: 10.1016/j.tins.2020.10.011. Epub 2020 Nov 21. PMID: 33234346; PMCID: PMC7855156.

CHOICE OF INDUCTION AGENT

- Does it really matter?
- Depends on the patient and physical examination
- Personnel preference also can be a factor
  - Comfort level and familiarity


70
60
50
40
30
20
10
0
% ADMINISTERED DOSE
Amount Metabolized
Muscle
VRG
Blood
Fat
1
3
10
30
100
300
TIME (MINUTES)

PROPOFOL

- Commonly used
- Enhances GABA activity via increased Cl- conductance causes CNS depression
- Rapid onset
- Minimal Excitement
- Good muscle relaxation
- Decreases ICP and CMRO2
- Hepatic and extrahepatic metabolism

PROPOFOL - DISADVANTAGES

- Cardiovascular side effects
  - Vasodilation
    - Blunts the increase in HR that should occur with vasodilation
  - Decreased Contractility
  - Sensitizes the heart to epinephrine induced arrhythmias
- Respiratory side effects
  - Hypoventilation
  - Apnea – rate of administration dependent
- No analgesia

PROPOFOL - DISADVANTAGES

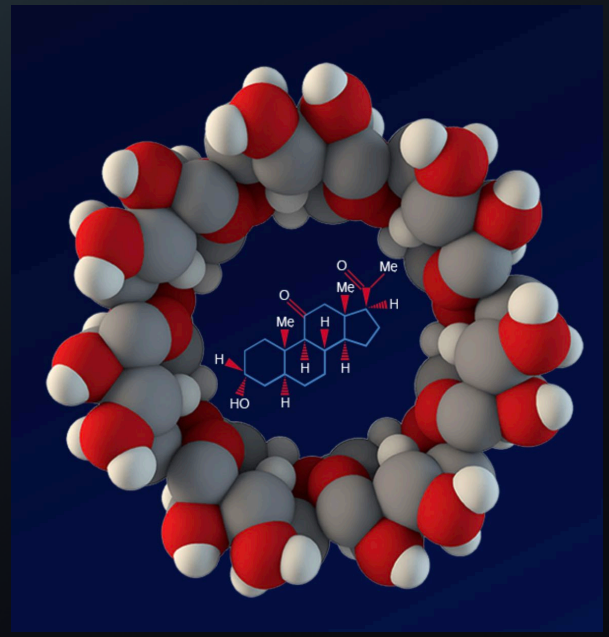
- Do they really matter?
- Time to think about co-induction options?

PROPOFOL – CATS

- Reports of repeated days of propofol induction causing anemia
- Oxidative RBC destruction
  - Heinz Body formation
- Lethargy
- Prolonged recoveries

ALFAXALONE

- Originally released in 1970s
- Formulation caused anaphylactoid reactions in humans and dogs
  - Saffan e.g. cremaphor
- Re-released in 2012 on the market with a new formulation
- Neurosteroid that enhances GABA receptor
- Not as broadly used as propofol
- Similar to propofol in its activity with some exceptions



ALFAXALONE – ADVANTAGES

- Rapidly acting
- Generally smooth induction quality
- Rapidly cleared by the liver
- Cats – No signs of anemia or lethargy after repeat doses
- Lower potential for bacterial contamination
- Decreases intracranial and intraocular pressure

ALFAXALONE – DISADVANTAGES

- Respiratory side effects (similar to propofol)
- Hypoventilation
- Apnea – rate of administration dependent
- Cardiovascular (Milder compared to propofol)
- Vasodilation with a compensatory increase in HR
- Some studies suggest that CO is maintained
- Myoclonus (Anecdotal reports of more frequent myoclonus, especially in cats)

ALFAXALONE – DISADVANTAGES

- Schedule 4 DEA controlled substance
- No analgesia
- Recoveries similar to propofol
- Reports of longer recoveries after prolonged administrations
- Cost

ETOMIDATE

- Introduced in 1983
- Enhances GABA activity
- Primary benefit is the minimal cardiovascular depression
- Maintains cardiac output
- Useful for patients with severe systolic dysfunction
- Probably worth referring those patients?

KETAMINE

- Ketamine approved for use in 1970
- Commonly used for many years
- Does not interact with GABA
  - Primary action through NMDA antagonism
- Acts through thalamocortical disassociation (commonly referred to as a dissociative)

KETAMINE

- Rapidly absorbed
- Has analgesic properties
- Can be given IV/IM/SC (may sting)
- Inexpensive
- Mild respiratory depression compared to propofol and alfaxalone

KETAMINE – CARDIOVASCULAR

- Increases in circulating norepinephrine
  - Increased HR
  - Vasoconstriction
  - May increase CO
- Advantage vs Disadvantage depends on patient

KETAMINE – DISADVANTAGES

- Caution with some types of cardiovascular disease
- Increase ICP
- Must be given with a muscle relaxant i.e midazolam or diazepam
- May be associated with dysphoric recoveries
- Metabolized to norketamine
- Caution in cats with kidney disease

TILETAMINE

- Similar advantages and disadvantages as Ketamine
- Comes packaged with a muscle relaxant
  - Zolazepam
- More potent and longer lasting than ketamine

CO-INDUCTIONS

- Using more than one induction agent or a sedative/analgesic agent to create an ideal anesthetic plane while minimizing the side effects
- Common Co-inductions
- Ketamine
- Fentanyl
- Lidocaine
- Midazolam?
  - benefit?

CO-INDUCTIONS - KETAMINE

- Has analgesic properties
- Minimal respiratory side effects
- Co-induction with propofol maintained higher MAP
- 0.5 to 1.0 mg/kg IV prior to induction agent

CO-INDUCTIONS – LIDOCAINE AND FENTANYL

- Reducing cough – Avoiding increases in ICP
  - Important for patients with head trauma or brain tumors

- Lidocaine (1-2 mg/kg IV)
- Evidence that an IV co-induction reduces cough on intubation
- Caution in cats
- Fentanyl (2-5 mcg/kg IV)
- May reduce cough as much or better than IV Lidocaine in dogs

CO-INDUCTIONS

- Midazolam???
- Minimal cardiovascular/respiratory side effects
- Commonly used as a co-induction with ketamine
- Combined with propofol
  - Should be given after the animal is effectively sedated
  - Did not improve hemodynamics in critically ill patients

CONCLUSION

- Induction implies start of GA with the onset of unconsciousness
  - Most dangerous time for anesthesia!
- IV induction agents are usually most efficient
  - Propofol
  - Alfaxalone
  - Ketamine/Tiletamine
- Co-inductions may reduce the negative side effects of using just one drug
- Specific procedures benefit from specific induction agents