

# Anesthesia Considerations in Rodent Biomedical Research

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## Anesthesia Types in Rodents

- Injectable (e.g. ketamine cocktails)
- Volatile gas (e.g. isoflurane, sevoflurane)
- Physical (e.g. hypothermia)

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## Why Anesthetize an Animal

- Avoid pain (loss of sensation)
- Immobilize (muscle relaxation)
- Avoid distress (loss of consciousness)

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## Injectable or Inhalation Anesthesia?



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## Injectable - Advantages

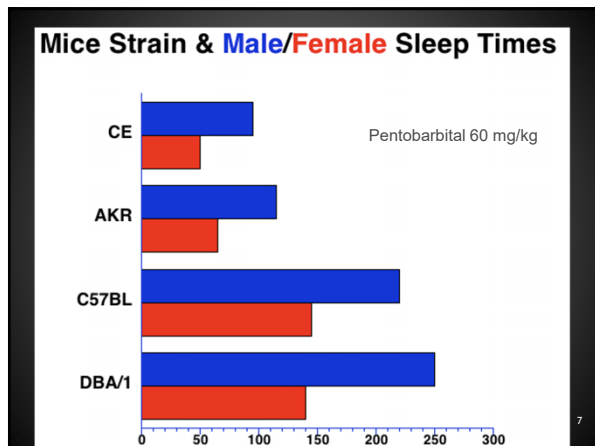
- Simple
- Cheap
- Minimal equipment

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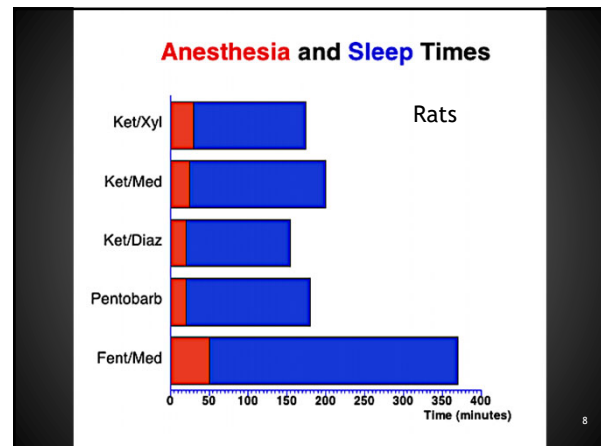
## Injectable Anesthetics - Disadvantages

- Higher morbidity & mortality
  - Hypoxic state
- Easier to overdose
- Slower induction and recovery
- Variable effects - Strain and gender differences

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### Inhalant Anesthetics - Advantages

Usually, suitable as sole agents to reach 'balanced' anesthesia

- Loss of sensation
- Loss of consciousness
- Muscle relaxation

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### Gas - Advantages

- Precise control over anesthetic depth
- Rapid induction/recovery
- Involves O<sub>2</sub>
- Greater consistency between strains and genders = experimental consistency

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### Gas - Disadvantages

- Anesthetic delivery system - \$\$\$???
- Requires a scavenging system
- Yearly calibration
  - Kent Scientific's *SomnoSuite* and *SomnoFlow* never require calibration

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### Gas Anesthetics

- Ether
- Halothane
- Methoxyflurane
- Enflurane
- Desflurane
- Isoflurane
- Sevoflurane

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## Isoflurane

- Decreases rate of production of cerebrospinal fluid (CSF)
- Increases rate of CSF absorption
- Most commonly used gas anesthesia in rodents

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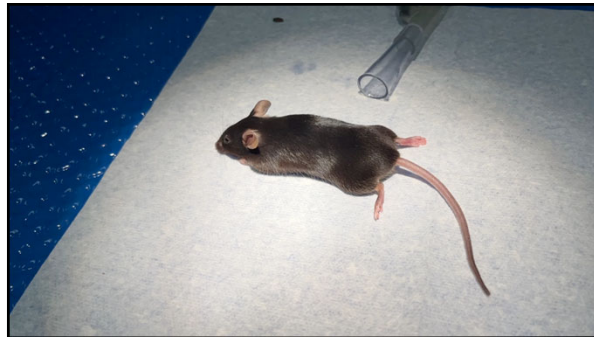
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## Isoflurane - Advantages

- Rapid induction/recovery
- Nearly 100% eliminated in exhaled air...
- Minimal cardiovascular depression
- Inexpensive... eventually!!!

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## Isoflurane Anesthesia Recovery

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## Isoflurane - Disadvantages

- Some respiratory depression
- Pungent odor may lead to breath holding in rabbits

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## Sevoflurane - Advantages

- Faster induction & recovery than isoflurane

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## Sevoflurane - Disadvantages

- Greater hepatic metabolism than isoflurane

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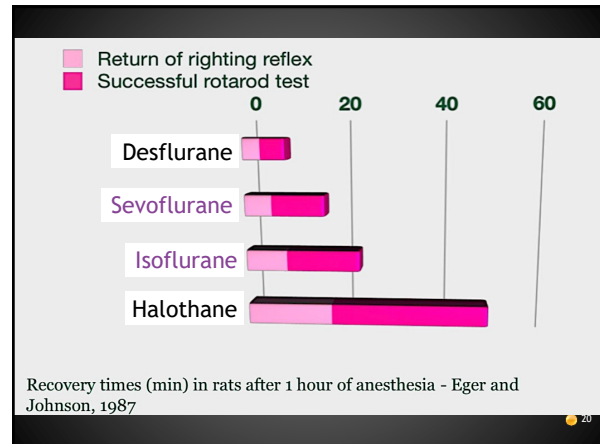
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## Anesthetic Gas Recovery as Metabolite<sup>1</sup>

- Methoxyflurane: 50%
- Halothane: 20-25%
- Enflurane: 2.4%
- Sevoflurane: 2-5%
- Isoflurane: 0.17%
- Desflurane: 0.02-0.2%

<sup>1</sup>Humans

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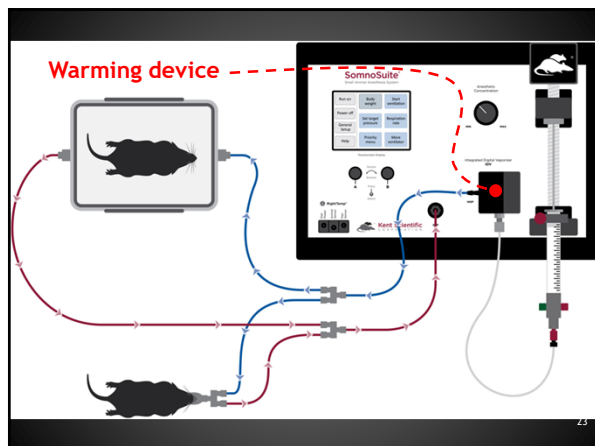
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### Somnosuite (Kent Scientific)

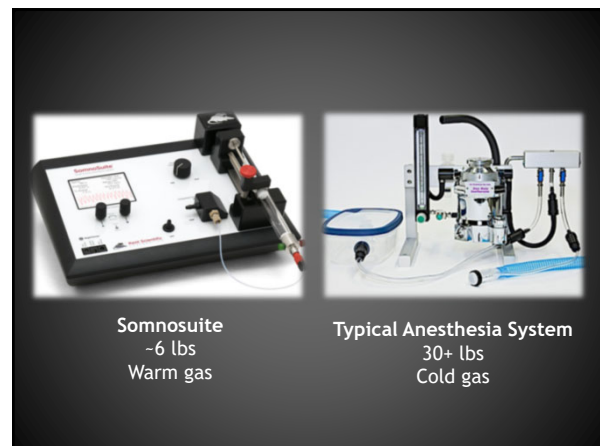
- Digital vaporizer
- Pre-warmed gas delivery
- Can deliver isoflurane and sevoflurane
- Temperature control
- Measures
  - Heart rate
  - Respiration rate
  - O<sub>2</sub> & CO<sub>2</sub>

No calibration required

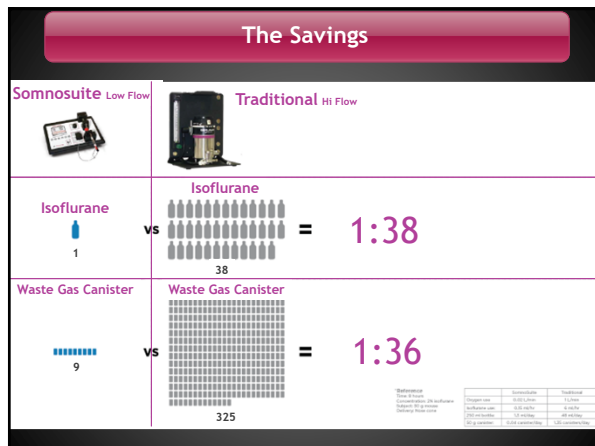
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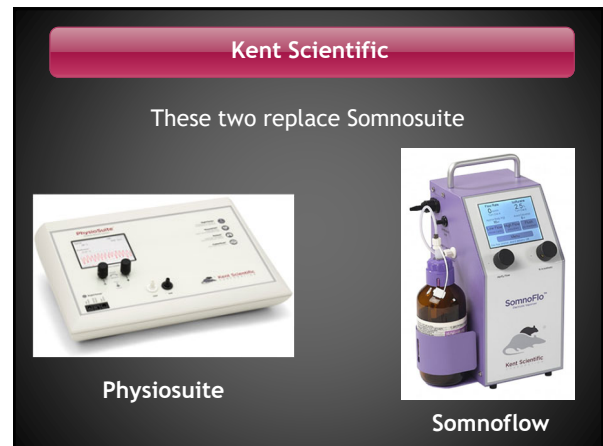
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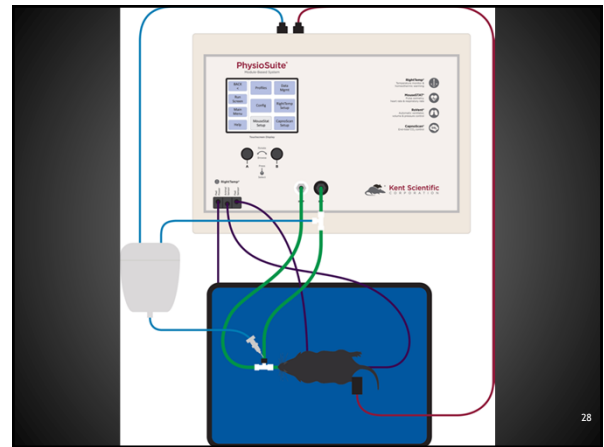
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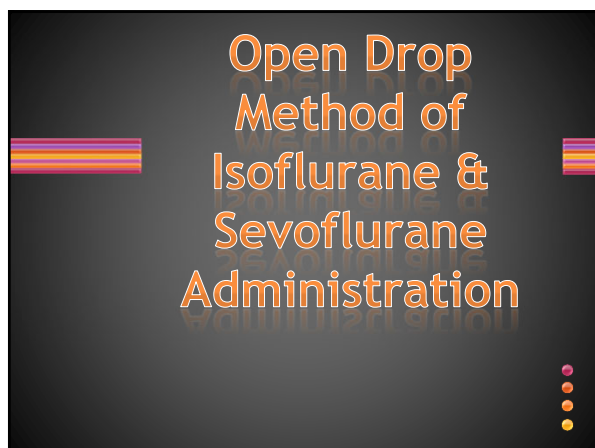
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## Open Drop

Useful & easy to apply, but...

- Must be vented out
- Prolonged use = deaths
- Used for very short-term anesthesia (minutes)

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## Mouse CPR



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## Open Drop Formula

Volume of liquid agent/ 1000 ml chamber volume	Approximate concentration of isoflurane
0.05 ml	1%
0.1 ml	2%
0.2 ml	4%
0.3 ml	6%

Replenish isoflurane every 3 mice

Emory University 33

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## Injectable Anesthetics

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## Pentobarbital - Advantages

- Placental transfer of barbiturates occurs rapidly. However, when used in proper induction doses, excessive depression of the fetus does not occur
- Administered IV or IP
- Neither hepato- or nephrotoxic

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## Pentobarbital - Disadvantages

- Pharmaceutical grade very pricey in US
  - High cost renders it "unavailable in pharm grade" \*\*\*
- Chemical grade use must be addressed & justified

\*\*\* NIH statement 2013

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## Pentobarbital - Disadvantages

- Prolonged recovery esp. if additional doses administered
- Severe cardiovascular & respiratory depression
  - Anesthetic & lethal doses close to each other... high mortality possible

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## Ketamine

- Cleared by hepatic metabolism
- By itself - poor anesthetic and analgesic in rodents
- Mix with other tranquilizers or sedatives ('cocktail')

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## Ketamine

- Cardio effects resemble sympathetic nervous stimulation - i.e. increased arterial BP, HR, CO, cardiac workload & myocardial oxygen consumption
- Such effects obtunded by prior or co-administration of tranquilizers or sedatives ('cocktail')
- Transient increase of norepinephrine & epinephrine in plasma

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## Ketamine - Advantages

- In hypovolemic patients, arterial BP is maintained with ketamine because of peripheral vasoconstriction
- No significant effect on hepatic or renal function
- Increases myocardial contractility

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## Ketamine - Disadvantages

- Increased airway & salivary secretions in some species (mild in mice & rats)
- Induces epileptiform bursts in thalamus & limbic system, but w/o spread to cortical areas
  - may increase seizure threshold in rats & mice
- Some respiratory depression following anesthetic doses in rodents (dose dependent obviously), worsened when used with sedative cocktail

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## Ketamine 'Cocktails'

- Safer, more 'balanced' anesthesia than pentobarbital or ketamine alone
  - Ketamine/xylazine
  - Ketamine/dexmedetomidine
  - Ketamine/xylazine/acepromazine

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## Ketamine 'Cocktail' Reversal

- Atipamezole shortens recovery time of ketamine/xylazine & ketamine/dexmedetomidine
- Atipamezole (0.5-1 mg/kg SC, IP, IM, IV) reverses xylazine & dexmedetomidine (not ketamine)
- Early reversal (10-20 minutes after induction) associated with undesirable behavioral disturbances due to effects of ketamine

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## Injectables

- Give lowest possible dose
- Supplement with oxygen

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## Ketamine/Medetomidine Reversal with Atipamezole



Courtesy of Dr. Paul Flecknell

Video Mouse - Anesthetic recovery w Atipamezole reversal

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Anesthetic  
recovery

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## Ketamine 'Cocktails'

- Use of yohimbine for reversal of ketamine/xylazine no longer recommended due to yohimbine's reported side effects
- For cocktail doses refer to <http://research.utsa.edu/research-funding/laboratory-animal-resources-center/training/>

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## Tribromoethanol (Avertin)

- Adequate anesthesia up to 30 min
- Repeat doses not recommended due to abdominal irritation & peritonitis reports
- Degrades in presence of heat or light - refrigerate, wrap in foil
- Non-pharmaceutical grade compound

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## Urethane

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## Urethane - Advantages

- IP Administration results in long-lasting unconsciousness of 6-10 hr
- Cardiopulmonary functions minimally affected, including blood pressure due to effects on catecholamine release
- Good analgesia for surgery in rodents

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## Urethane - Disadvantages

- Peritoneal effusion & hemolysis
- Mutagen/carcinogen
- Readily absorbed through skin
  - pre-neoplastic changes in skin
  - targets multiple organs
  - suppresses bone marrow
  - readily crosses the placenta
  - fetal tumor formation (*in utero*)

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## Urethane

- Strict guidelines (gloves, mask, prepare in fume hood)
- Not used for survival surgeries

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## Resources

Presentations, References & Useful Notes  
<https://research.utsa.edu/compliance/larc/training.html>  
[www.plavs.net](http://www.plavs.net)

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