



Medizinische Universität Graz

SHEEP AS BIOMODEL

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Sheep as experimental animals (1 / 3)

- ▶ No “traditional” lab animal (familiarity)
- ▶ Larger animals required for some types of experiments
 - ▶ Dog (traditional, ...repugnant? expensive?)
 - ▶ Farm animals (ready supply) → pig, sheep, goat (sheep + goat very similar in nearly all aspects)
- ▶ Sheep sometimes appear to be very alien animals to people with no vet / agricultural background, but actually are very easy to manage + to use for experimentation



Sheep husbandry

Indoors:

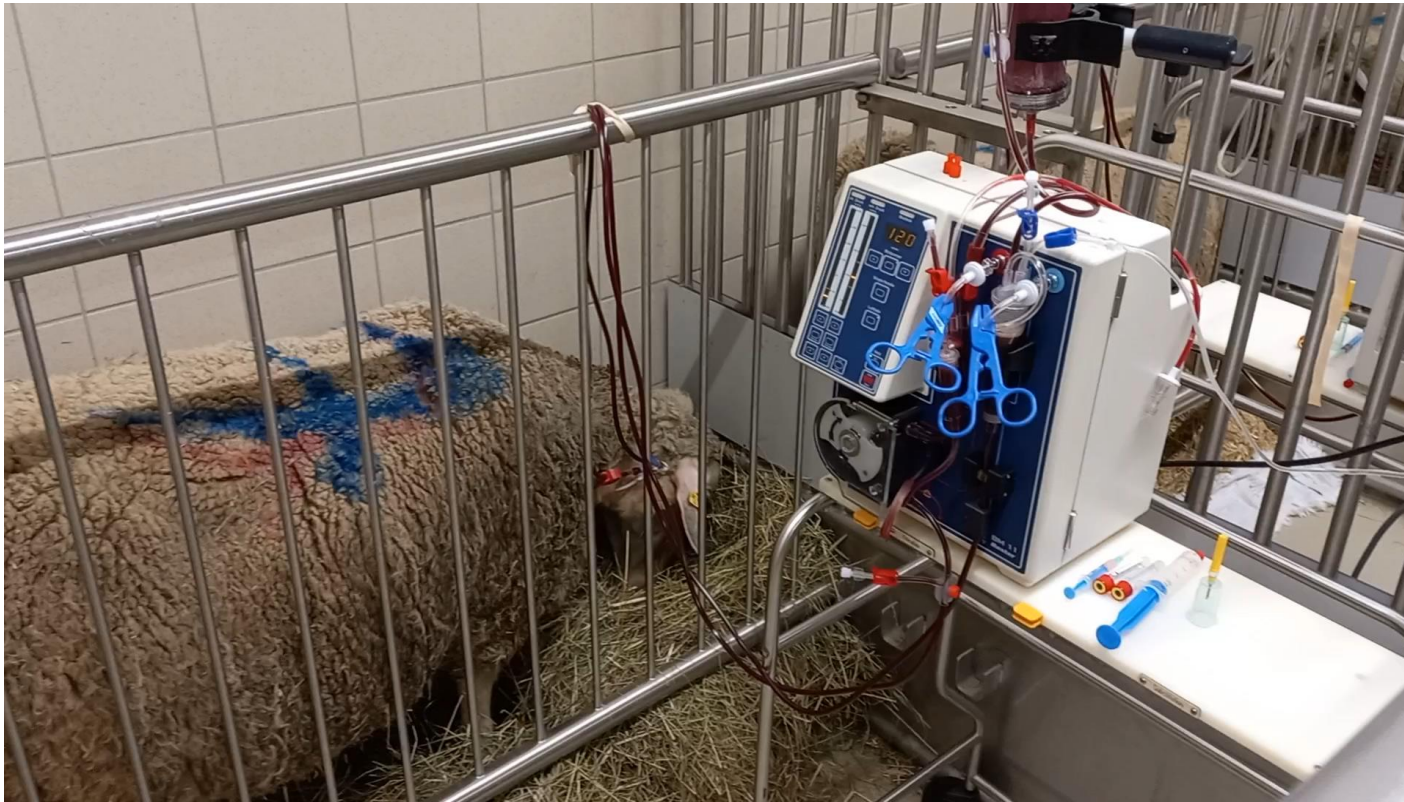
- ▶ Sheep are kept in flocks, mostly in pens - appropriate for this species
2 m² / sheep
should allow sheep to turn around and to lie down with ease
- ▶ UV insect traps
- ▶ Single housing only if necessary for therapy or experiment

Outdoors:

- ▶ in flocks with access, throughout the day,
to an external weather-proof stall and to the adjacent sheep meadow



Training



Sheep as experimental animals (2/3)

History:

- ▶ 1667 transfusion incompatibility
- ▶ 1790 Dr. Guillotin perfected his “machine” on sheep (French Revolution)
- ▶ 1863 thrombus formation on intravascular devices
- ▶ has become widely used for research + its use continued to increase
- ▶ → 3 main areas...



Life support machine
for
cardiopulmonary resuscitation



Sheep as experimental animals (3/3)

- I. **Agricultural** type of research (diseases, parasites, nutrition, breeding, reproduction, growth,...)
- II. **Medical** research → to obtain a better understanding of human disease and its treatment
 - 1. Similar size to man (“70-80 kg”)
 - 2. Suitability for chronic experimentation after surgical modification (≠ pig)
- III. **General biological knowledge**
 - 1. Hemoglobin switching (peculiar to sheep)
 - 2. Lymphatic + fetal studies
 - 3. Purification of sheep hormones
 - 4. Use of sheep red cells in immunology



Anesthesia protocol (1/2)

Depends on:

- ▶ planned intervention
- ▶ experimental protocol (influence on result?)
- ▶ experimental conditions (equipment, personnel, experience,...)



Anesthesia protocol (2/2)

- ▶ Attention when choosing the anesthetic and the mode of application!
- ▶ Stress sensitive (especially when isolated from flock)
- ▶ Prone to vasospasms when under stress
- ▶ Very sensitive lung tissue:
(damage due to over-inflation during mechanical ventilation)
- ▶ Could lead to pulmonary edema



Preparation of patients

- ▶ Clinical examination (cardiorespiratory function)
- ▶ Fasting is very difficult (polygastric animals)
- ▶ Weight (polygastric animals)
- ▶ Blood parameters (Hk, Tp, blood count, blood chemistry, blood gases) depending on the procedure

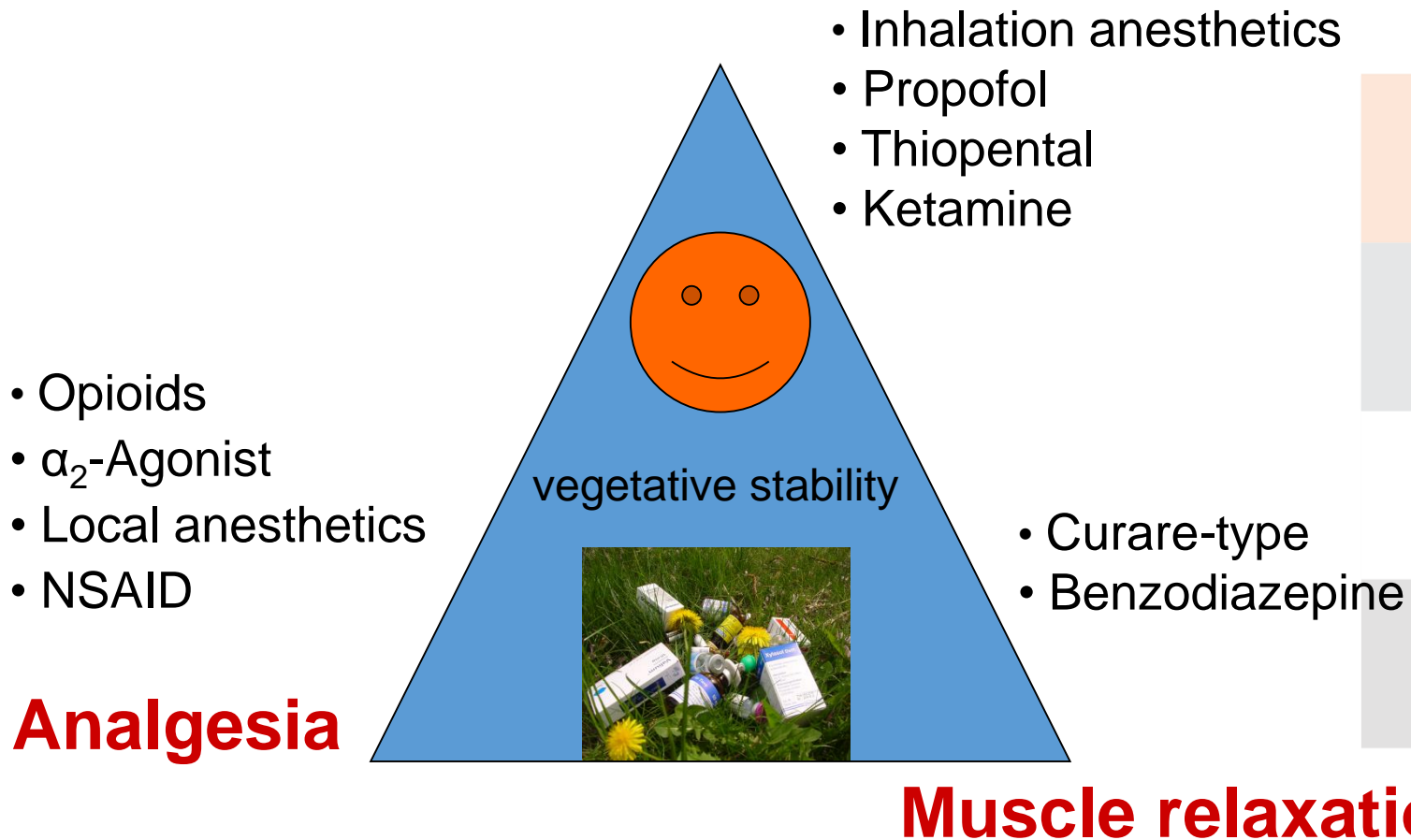


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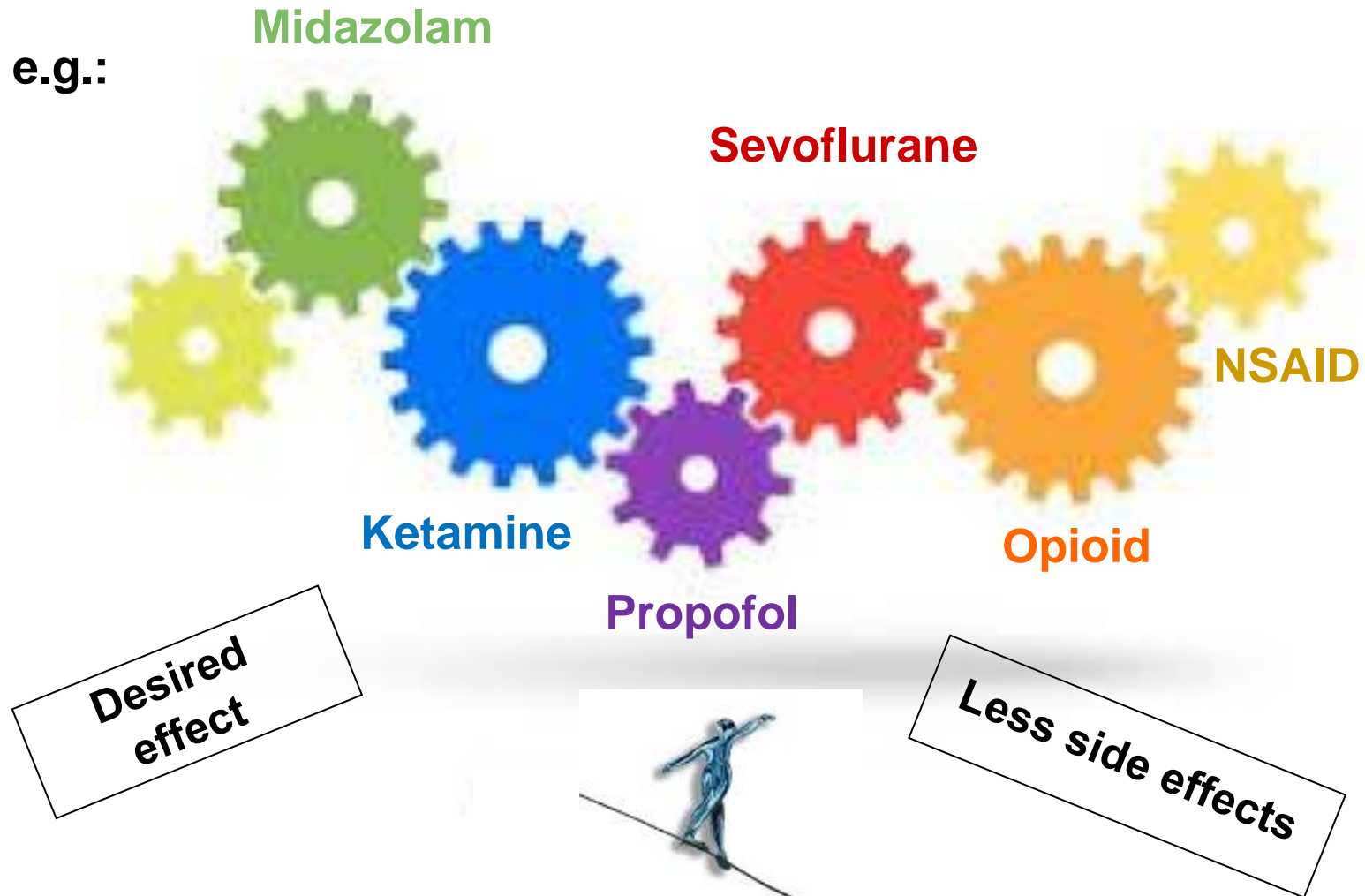


What is general anesthesia?

Unconsciousness / Insensibility

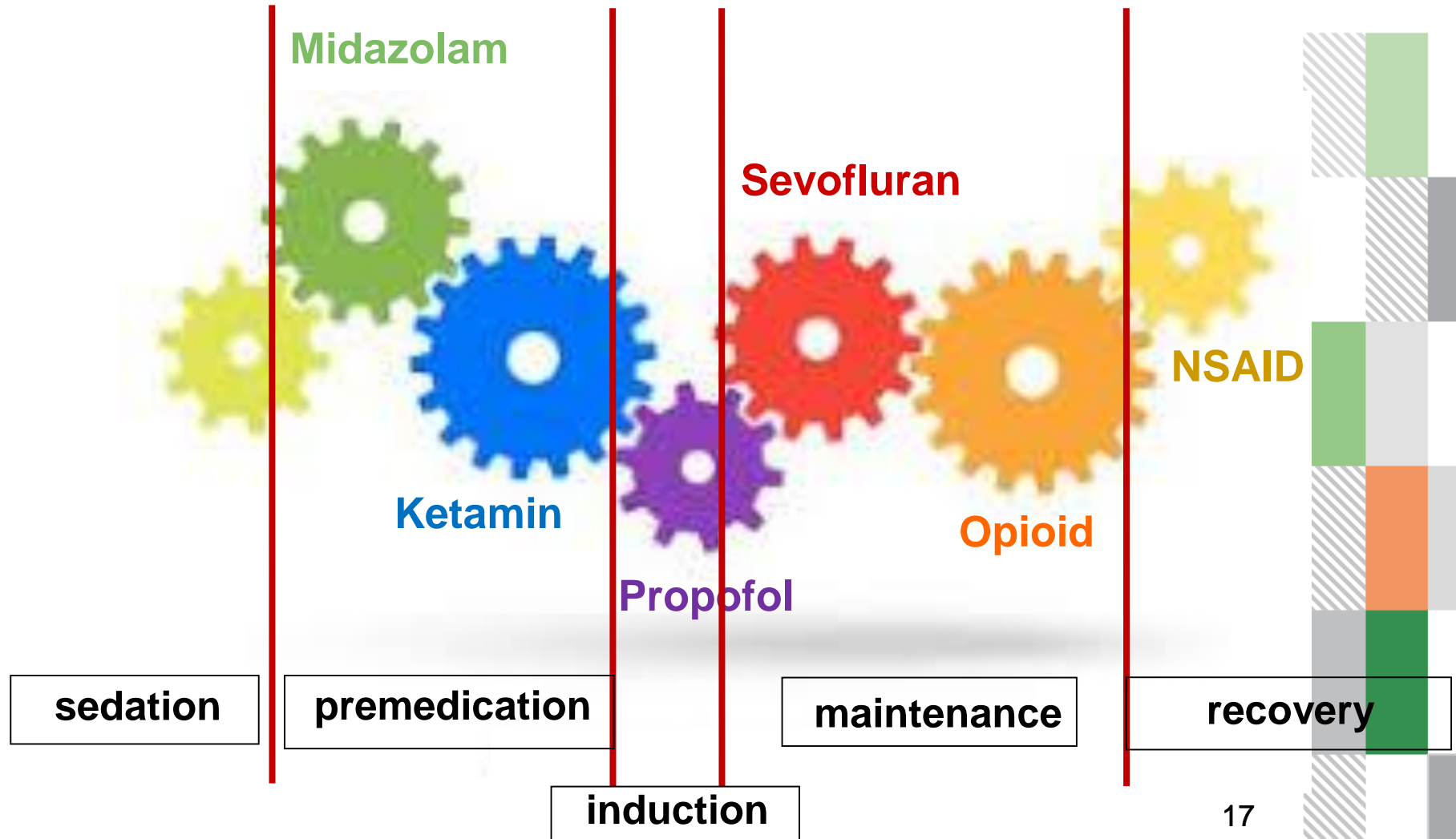


Balanced anesthesia





Phases of anesthesia



Sedation and/or with premedication (1/4)

- ▶ Stress reduction, anxiolysis, sedation
- ▶ Gentle induction, stable maintenance + recovery phase
- ▶ Dose reduction of general anesthesia
- ▶ Analgesia

Injections:

- ▶ i.v.
- ▶ s.c. and i.m.
only for sedation
(unreliable onset of action)



Cannula placement

► V. auricularis

► V. jugularis



Sedation and/with premedication (2/4)

Benzodiazepine

- ▶ central muscle relaxant
- ▶ sedation level very good
- ▶ almost without effect on cardiovascular / respiratory system
- ▶ combinations with ketamine (+/- opioids)

Midazolam 0.1 - 0.5 (-1) mg/kg i.v.



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Sedation and/with premedication (3/4)

Ketamine

- ▶ Dissociative anesthetic
- ▶ Catalepsy
- ▶ Analgesia (musculoskeletal and neuropathic pain, anti-hyperalgesic)
- ▶ Increases hemodynamic parameters
- ▶ Without influence on respiration, **increased bronchial secretion**
- ▶ Hyperthermia
- ▶ Intracranial blood flow increases - and so does intracranial pressure
- ▶ Swallowing reflex preserved, **no aspiration protection**
- ▶ 2 - 5 mg/kg i.v.



Sedation and/with premedication (4/4)

- ▶ **$\alpha 2$ - Agonists**
- ▶ Xylazine may cause acute lung embolism by i.v. application
- ▶ **Attention!!!**
- ▶ Dose: 0.05- 0.1 mg/kg i.m. combined with ketamine 2mg/kg for short anesthesia or premedication for general anesthesia



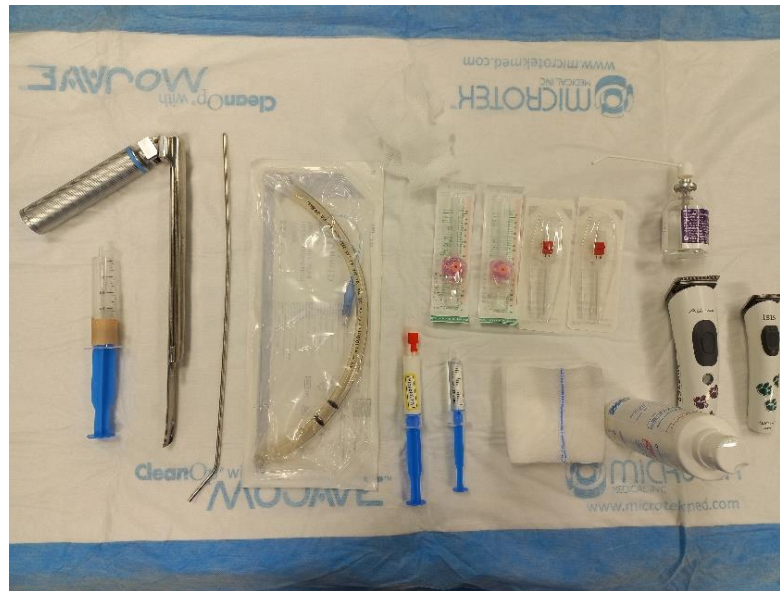
Induction of general anesthesia

- ▶ Ketamine 2-5 mg/kg i.v.
 - ▶ **Propofol 0.5 - 2 mg/kg i.v. (on effect)**
 - ▶ Loss of jaw tension, **eyelid reflex is not meaningful**
 - ▶ Intubation (by adequate depth of anesthesia)
-
- ▶ Sheep are susceptible to apnea
 - Oxygenation (Mask)
 - Quick intubation



Intubation (1/2)

- ▶ More difficult than in other animals
 - ▶ Length of oral cavity
 - ▶ Head form
 - ▶ Cleft palate is narrow
 - ▶ Breast belly position
- (extra long laryngoscope; endotracheal tube)



Intubation (2/2)

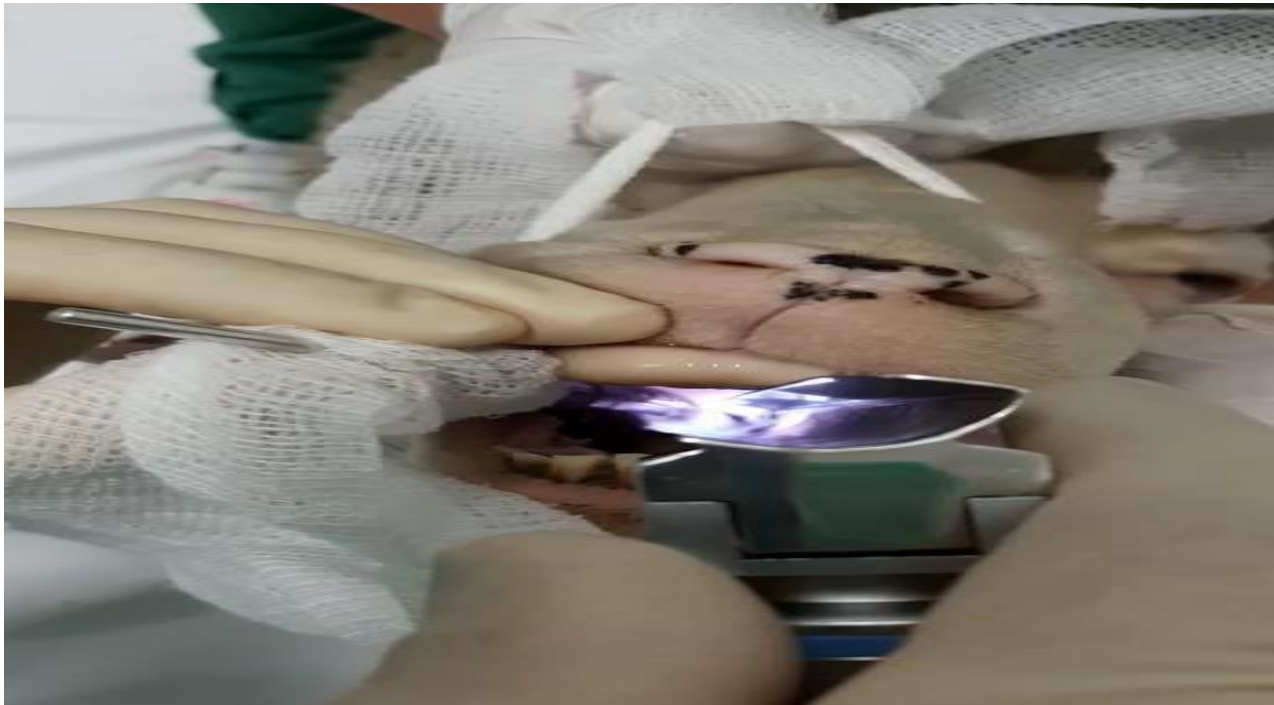
- ▶ Always under supervision!
- ▶ Advance the tube with a rotating forward movement (corkscrew-like)
- ▶ No unnecessary high pressure!



Intubation



Intubation



Maintenance of general anesthesia

► Inhalation anesthetics

Isoflurane

Sevoflurane

► Continuous infusion i.v.

Fentanyl 30-50 mcg/kg/h

Propofol 2-4 mg/kg/h

Ketamine 1-5 mg/kg/h

Fluid substitution!!!!

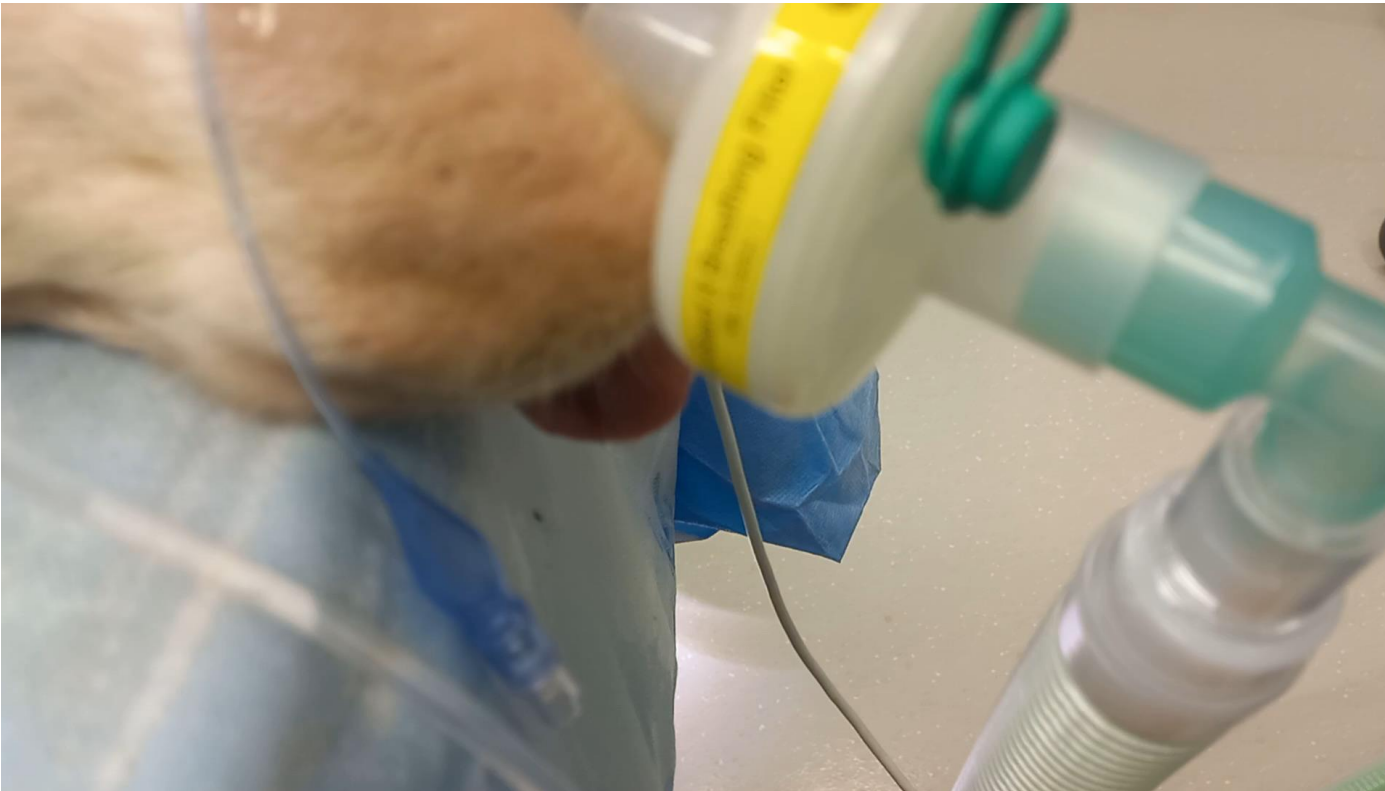


Clinical monitoring of sheep

- ▶ Salivation
- ▶ Regurgitation **cave!**
- ▶ Respiratory pneumonia
- ▶ Tracheal lumen is often larger than max. lumen of usual commercial tracheal tubes
- ▶ Chest is very deep
- ▶ High pressure from rumen to lung
- ▶ Spontaneous breathing is impossible
- ▶ Gastric distension during anesthesia especially in back position



Salivation



Recovery

- ▶ Recovery phase mostly calm, no early attempts to stand up
- ▶ Postoperatively, high risk of respiratory arrest!
- ▶ Extubation only when clear swallowing and chewing
- ▶ Oxygen!
- ▶ Frequent and conscientious control of the cardiovascular system
- ▶ Hypothermia - prevention
- ▶ Analgesia BEFORE perception of pain
(reduces complications like:
hypoventilation, hypercapnia, hypoxemia...)
- ▶ Infusions
- ▶ Suction!!!!!!



Pain detection by sheep (1/2) (general behavior changes)

- ▶ Reduced feed intake and rumination
- ▶ Licking, rubbing or scratching painful areas
- ▶ Reluctance to move
- ▶ Grinding their teeth and curling their lips
- ▶ Altered social interactions
- ▶ Changes in posture to avoid moving or contacting a painful body area



Pain detection by sheep (2/2)

Orbital tightening – there is a closing of the palpebral fissure by the eyelids and a narrowing of the eye aperture

Cheek tightening – there is a more convex shaping to the cheek in the area of the masseter muscle

Abnormal ear posture – ears become fully rotated ventrally and caudally

Abnormal lip and jaw profile – the jaw profile appears straight to concave

Abnormal nostril and philtrum shape – a “V” shape between nostril apertures is present



Analgesia

- ▶ NSAIDs (Carprofen, Metamizole, Meloxicam,...)
 - ▶ Opioids (Butorphanol, Buprenorphine, Morphine, Methadone, Fentanyl,...)
 - ▶ Ketamine
 - ▶ Tramadol
 - ▶ Local anesthetics
- ...multimodal pain treatment!**

careful with dosage and interval

WHO-Stufenschema zur Schmerztherapie



Carprofen 2-4 mg/kg



0.1-0.3 mg/kg



25 – 100 µg/kg/h

Thank you for your attention



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