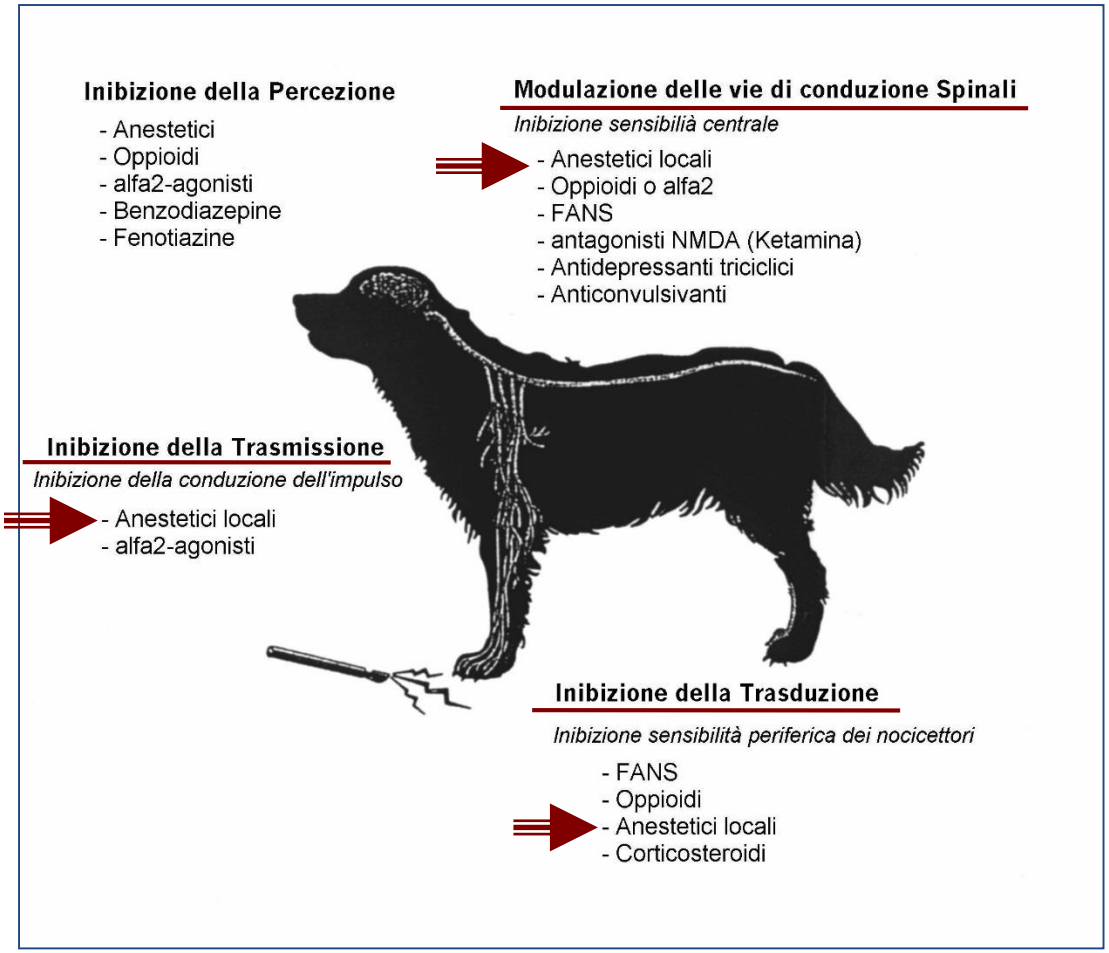
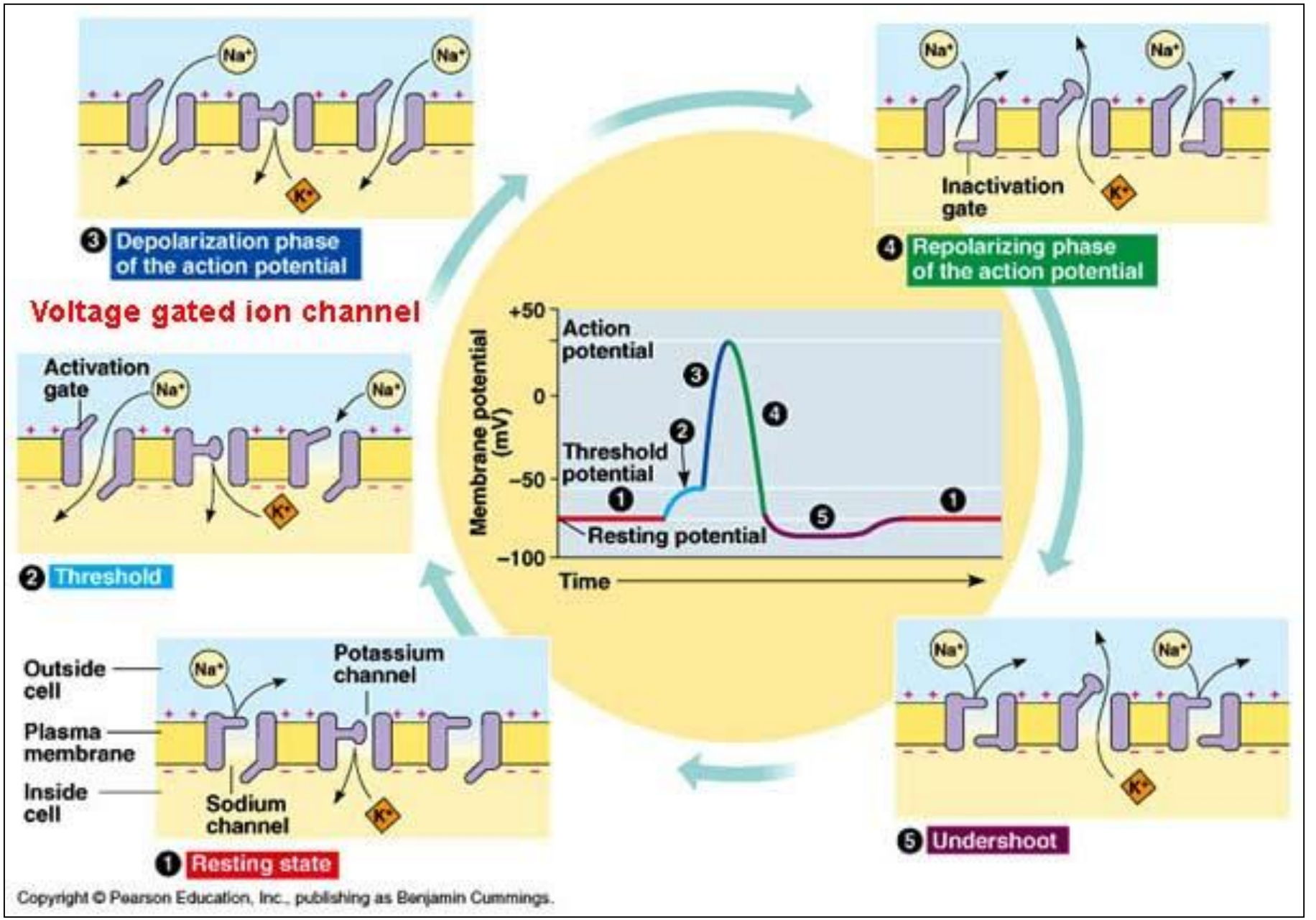
Local Anesthetics

- Decrease or prevent Na+ permeability of the membrane of neurons, which stops the transfer of signals along the peripheral nerves
- Prevent central sensitization since the nociceptive signal is blocked
- Classified by duration of action
  - Lidocaine is short acting with a rapid on-set
  - Bupivicaine is long acting with a slow on-set
  - Duration of action can be extended by adding a vasoconstrictor like epinephrine

Local anaesthetics

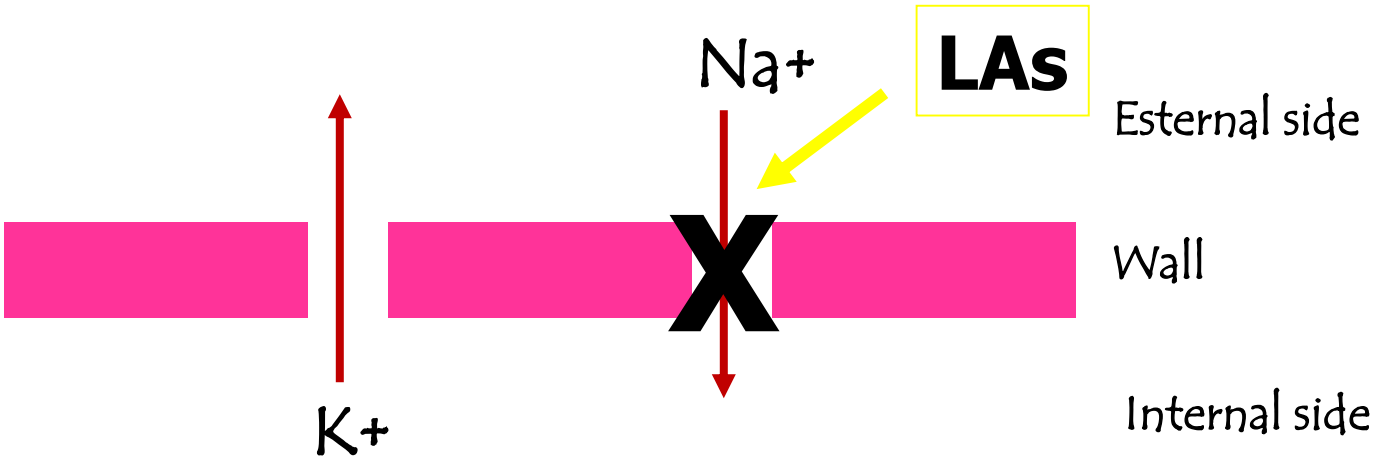
prevent or eliminate pain by the block of the pain signal transmission though nerve fibres

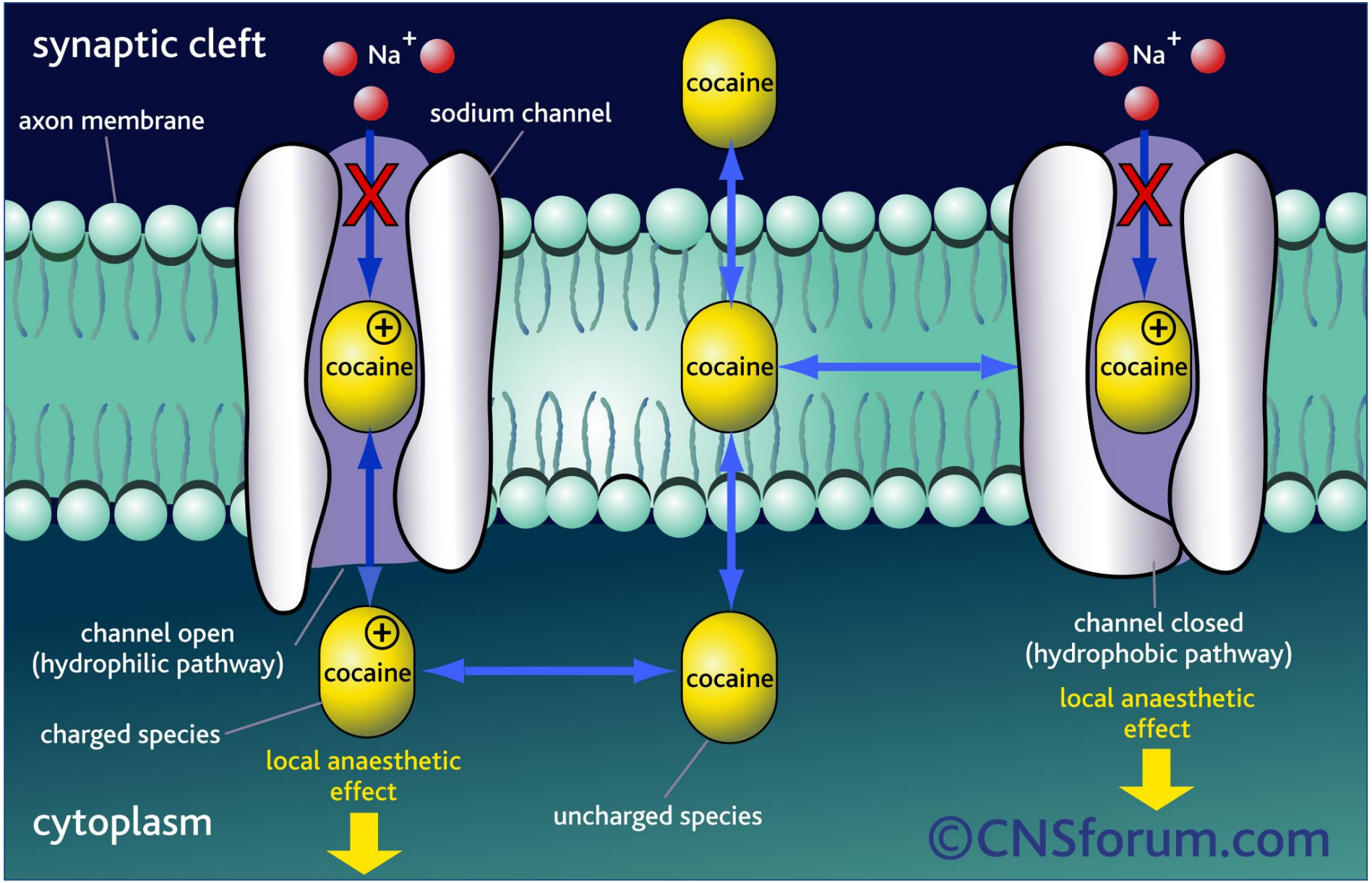




Mechanism of action

- LAs inhibit generation and propagation (conduction and transmission) of electric signals by the blockage of Na^+ channels




synaptic cleft
Na+
Na+
axon membrane
sodium channel
cocaine
cocaine
cocaine
cocaine
cocaine
cocaine
channel open
(hydrophilic pathway)
charged species
local anaesthetic
effect
uncharged species
channel closed
(hydrophobic pathway)
local anaesthetic
effect
cytoplasm
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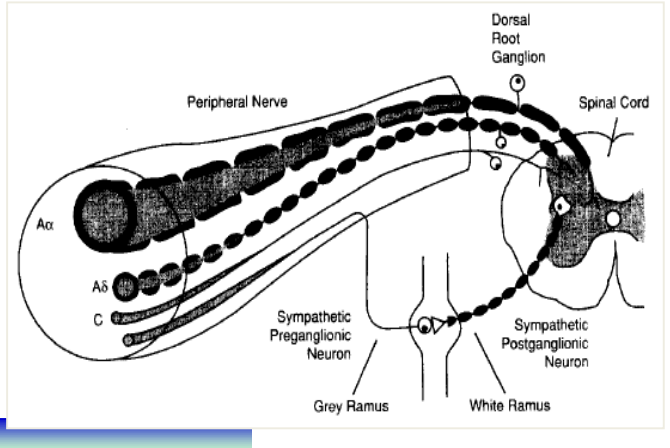
Diameter of nerve fibres and the myelin degree play an important role in conduction of the electric signals and influence the sensitivity to LAs



Fibre A myelinated

Aα Ø 6–22 µ 1,2 mm somatic-motor proprioception

Aβ Ø 5–12 µ 0,8 mm somatic-motor proprioception

Aγ Ø 3–6 µ 0,5 mm muscular tone

Aδ Ø 2–5 µ 0,2 mm pain, temperature, tact

Fibre B myelinated Ø < 3 µ 0,1 mm autonomic functions *preganglionic sympathetic*

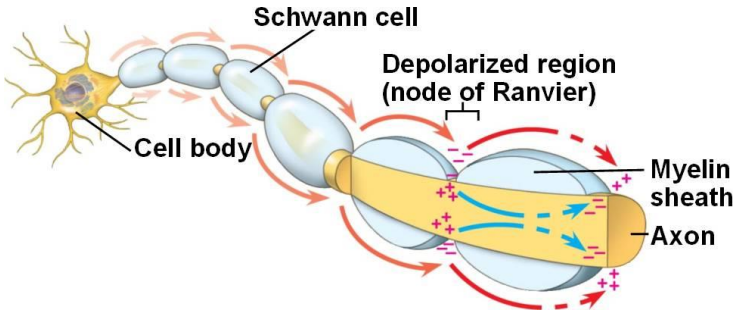
Fibre C unmyelinated Ø 0,4–1,3 µ pain, temperature, tact
autonomic functions *postganglionic sympathetic*

Larger the diameter higher the amount of LAs to obtain a nerve blockage.

Generally:

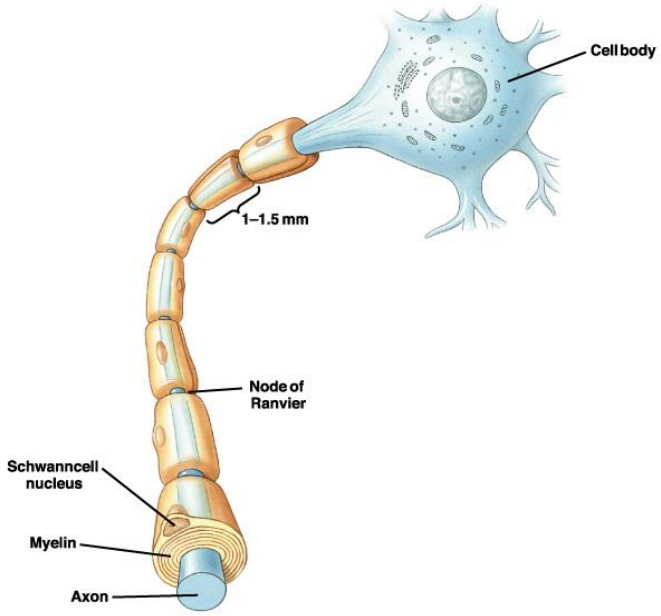
a) Small fibres C *(small diameter, unmyelinated)* and Aδ *(small diameter, myelinated)* are blocked before
b) Fibres Aα, Aβ, e Aγ *(larger diameter, myelinated)* are blocked later

It is unlikely that the size of fibres can itself determine the sensitivity to LAs blockages



In the myelinated fibres the electric signal moves from a node of Ranvier to the next *(saltatory conduction)*

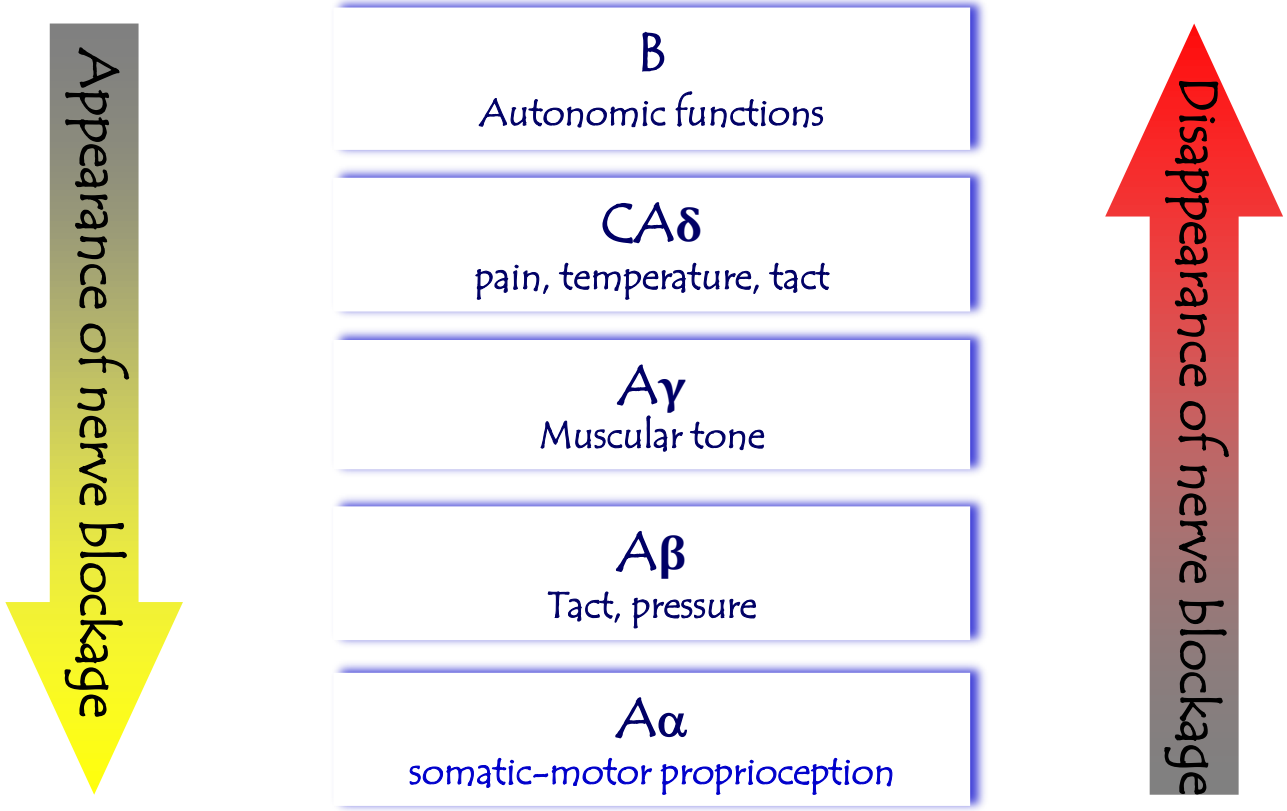
A complete anaesthesia is achieved with the consecutive blockage of at least 3 nodes of Ranvier



The distance between two nodes increases if the diemeter of the fiber increases

The small fibres with nodes of Ranvier closer could be blocked more rapidly

Sensitivity to LAs



The different sensitivity of nerves to LAs allows to obtain a diverse inhibition of sensory inhibition compared to the motor

Disappearance of nerve functions sorted by sensitivity to LAs:

1. Pain
2. Heat
3. Touch
4. Pressure
5. Motor function

Thanks to these differences in sensitivity the LAs can block the sensory transmission without the motor paralysis

Local Anesthetics

Multiple uses and routes of administration

- Topical: most are applied to mucous membranes but some preparations will be absorbed through skin
  - 0.5% proparacaine is recommended for examining eyes
  - Lidocaine and benzocaine sprays are used to assist in intubation (benzocaine has been implicated in methemoglobinemia and should be used sparingly and with caution)
  - Xylocaine jell can be used to lubricate endotracheal tubes and urinary catheters
  - EMLA cream contains lidocaine and prilocaine and is used to numb skin

Local Anesthetics

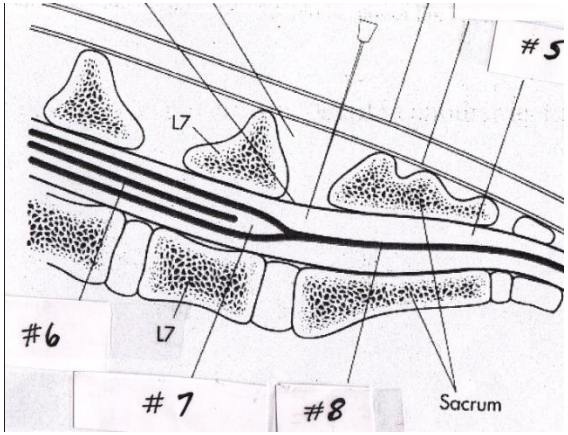
- “Splash”
  - Can apply to exposed tissues prior to closure and nerves prior to transection during amputations
  - “Soaker catheters”
- Infiltration
  - Multiple intradermal or subcutaneous injections of local anesthetic along proposed incision line
  - May contain epinephrine (1:200,000) to increase effect and duration
- Field block
  - Used to anesthetize large areas
    - Intradermal or SQ infiltration followed by injection deeply enough to infiltrate nerves

Local Anesthetics

- Regional blocks (nerve blocks)
  - Injection into the connective tissue surrounding a nerve
  - Can produce loss of sensation and/or paralysis in the region supplied by the nerve
  - Requires smaller volumes than field blocks, reducing the risk of toxicity

Local Anesthetics

- Epidurals
  - Administered alone or in combination with other analgesics
  - If combined, smaller doses can be used, decreasing risks of adverse effects
  - Can cause motor deficits at higher doses



Tricaine methanesulfonate for anesthesia of fish

- Anesthetics are used to sedate fish during transport or handling, and immobilize fish for surgical procedures by depressing their central and peripheral nervous systems.
- TMS is the only legal anesthetic for use on a limited number of food fish (FDA 2006). The limitations on TMS use with food fish include a 21-day withdrawal period before harvesting.
- Different legislations among countries

Tricaine methanesulfonate safety use

- TMS is a white, odourless crystalline powder with a high solubility in water (1 g/0.8 mL of TMS at 20°C)
- TMS in powder form easily can become airborne and could become hazardous to the handler
- TMS is retinotoxic and an irritant to mucous membranes, including the upper respiratory tract
- TMS is generally prepared as a concentrated stock solution
- TMS solution is photosensitive (brown bottle 3-month activity)

Tricaine methanesulfonate

- Although classified as a local anesthetic, TMS acts systemically when absorbed through the gills and

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RESEARCH PAPER

A review of tricaine methanesulfonate for anesthesia of fish

Kathleen M. Carter · Christa M. Woodley · Richard S. Brown

Alpha$_2$-Adrenergic Agonists

- Stimulation of the alpha$_2$ – adrenoceptors result in sedation, muscle relaxation, and analgesia
- Can be reversed with alpha$_2$-adrenergic antagonists such as yohimbine and atipamezole
- Includes xylazine, medetomidine, and detomidine

Miscellaneous Analgesics

- Ketamine
  - NMDA antagonist
  - Used as a CRI during surgery at sub-anesthetic doses, it reduces MAC and can help prevent hypersensitivity
  - More effective treating somatic pain than visceral pain
  - Can be administered via epidural injection
- Gabapentin
  - Analogue of naturally occurring neurotransmitter GABA
  - Believed to increase production of GABA
    - Part of endogenous inhibition of nociception
  - Used to treat nerve pain

Why is clearance a fundamental PK parameter ?

Clearance is the only parameter measuring the ability of a body (or an organ) to eliminate a drug

Ability is not synonymous with rate of elimination (i.e. dx / dt)

Why clearance should be evaluated ?

- for a practical purpose: dose computation

- for a mechanistic purpose: interpretation

Is a Penicillin G plasma clearance of 8.5 mL /kg/min high, low or very low?

Is a Penicillin G plasma half-life of 0.88 h short, long or very long ?

Is a Penicillin G plasma clearance of 8.5 mL /kg/min high, low or very low?

Difficult to answer because clearance has the dimension of a flow

Is a Oxytetracycline plasma clearance of 0.42 mL /kg/min in rainbow trout high, low or very low ?

Is a Oxytetracycline plasma half-life of 81.2 hours in rainbow trout short, long or very long ?

Plasma clearance

$$Cl = \frac{dx/dt}{C} = Q \times E = \frac{Dose}{AUC}$$

Definition

Model

Computation model

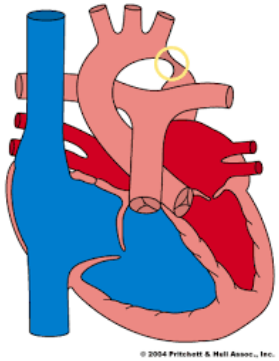
Concepts not to confuse

What reference system for plasma clearance?

Reference system: clearance vs half-life

Plasma clearance

(L/min/kg)



Cardiac output

Plasma half-lifr

(minutes)

Watch

The body (blood) clearance

- Model to interpret blood clearance

$$Cl_{body} = Q°_{cardiac\ output} \times E_{body}$$

flow flow no unit

- Operationally, clearance is the blood (plasma) volume which is totally cleared of the analyte during a time unit

Interpretation of body clearance

- Interpretation of body clearance consists of calculating an extraction ratio

$$E_{body} = \frac{\textbf{Body clearance (blood)}}{\textbf{Cardiac output}}$$

Cardiac output

- From literature
- From allometric relationship

$$\mathbf{Q° \ (mL/kg/min) = 180 \ BW \ (kg)^{-0.19}}$$

- Example : a 500 kg BW horse

- $Q° = 180 \times 500^{-0.19} = 180 \times 0.307 = 55.3$ mL/kg/min

Is the Penicillin G plasma clearance high or low ?

- **body clearance 8.5 mL/kg/min**

- cardiac output: ≈55 mL/kg/min
- extraction ratio: ≈15.4%

Application of the clearance concept

Interspecies comparison

Interpretation of the body clearance

Is the body clearance (ml/kg/min) high, medium or low?

							
BW, (kg)	0.2	3	10	50	70	100	500
Cl high (E=0.35)	85	51	41	30	28	26	19.4
Cl medium (E=0.15)	37	22	17.4	13	12	11.3	8.25
Cl low (E=0.05)	12.2	7.3	5.8	4.3	4.0	3.75	2.75

Application of the clearance concept

Interspecies comparison

BW	Plasma (blood) Clearance (mL/kg/min)	Cardiac Output (mL/kg/min)	Extraction ratio
10 g	107	430	0.25
20 Kg	25	100	0.25
80 kg	19.5	78	0.25

Conclusion : all three species had the same overall capacity to eliminate the drug

Application of the clearance concept

Interspecies dose extrapolation

Interspecies dose extrapolation

- **Goal : to obtain the same exposure (AUC) for the 2 species**

Dose = AUC x Cl

$$AUC_{man} = AUC_{rat} = \frac{Dose_{rat}}{Cl_{rat}} = \frac{Dose_{man}}{Cl_{man}}$$

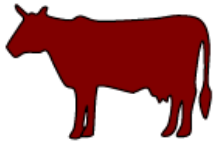
$$Dose_{man} = \frac{Cl_{man} \times Dose_{rat}}{Cl_{rat}}$$

Dose extrapolation

$$\text{Dose}_{\text{species1}} = \frac{\text{Dose}_{\text{species2}} \times \text{Cl}_{\text{species1}}}{\text{Cl}_{\text{species2}}}$$

Interspecies dose extrapolation

Which dose of ketoprofen in goat ?



: 3 mg/kg/24 h ; Cl = 0.17L/kg/h

: Cl = 0.74 L/kg/h

$$Dose_{goat} = \frac{Dose_{cattle}(3mg/kg) \times Cl_{goat}(0.74L/kg/h)}{Cl_{cattle}(0.17L/kg/h)}$$

$Dose_{goat}$ = 13 mg/kg

Table II. Anesthetics and Analgesics used in Mice

Anesthesia in Mice	Dose & Route	Comments
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	35 mg/kg IV 40 – 70 mg/kg IP	Caution! Potentially significant cardiovascular and respiratory depression, variable response
Thiopental	50 mg/kg IP; 25 mg/kg IV	
Tribromoethanol (Avertin)	125-250 mg/kg IP	Store at 4°C; dark conditions
Ketamine + Xylazine	100 mg/kg (K) + 10 mg/kg (X) IP	
Ketamine + Medetomidine	75 mg/kg (K) + 1.0 mg/kg (M) IP	
Ketamine + Xylazine + Acepromazine	100 mg/kg (K) + 20 mg/kg (X) + 3 mg/kg (A) IP	
Hypothermia (Neonates <4 days old undergoing minor surgical procedures only)	Submerge for 3 – 4 minutes in ice water	Pup placed in rubber sleeve, submerged to cervical area with resultant 10 minutes of anesthesia
Analgesia in Mice		
Morphine	1 – 10 mg/kg SC	Up to 3 hours of analgesia
Oxymorphone	0.05 mg/kg SC	Up to 3 hours of analgesia
Meperidine	10 – 20 mg/kg SC	Up to 3 hours of analgesia
Imipramine	2 – 3 mg/kg SC	Up to 12 hours of analgesia
Butorphanol (Torbutrol® 0.5mg/ml)	0.05 – 5.0 mg/kg SC	1 – 2 hours of analgesia
Buprenorpnine (Buprenex®)	0.05 – 2.0 mg/kg SC	3 – 5 hours of analgesia; do not use with tribromoethanol
Pentazocine	10 mg/kg SC	Up to 4 hours of analgesia
Carprofen	10 mg/kg SC	From 12 - 24 hours of analgesia
Ketoprofen	10 mg/kg SC	From 12 - 24 hours of analgesia
Sedation in Mice		
Medetomidine	30 – 100 µg/kg SC	Reverse with Atipamezole @ 1.0 µg/kg SC, IP, or IV
Ketamine	44 mg/kg SC	
Chlorpromazine	5 – 10 mg/kg SC	

Note: Mice have a relatively small total muscle mass and are prone to develop muscular atrophy or nerve damage following IM injections. The IM route should be avoided in mice. If drugs must be administered via the IM route, minimal injection volumes (≤0.05 ml), and a 27-30-gauge needle should be used.

Table III. Anesthetics and Analgesics used in Rats

Anesthesia in Rats	Dose & Route	Comments
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	30 – 40 mg/kg IV 40 – 60 mg/kg IP	Caution! Potentially significant cardiovascular and respiratory depression, variable response
Thiopental	20 – 40 mg/kg IV 40 mg/kg IP	5 – 10 minutes of anesthesia
Ketamine + Xylazine	60 – 90 mg/kg (K)+ 6 – 9 mg/kg (X) IP	30 – 45 minute duration; may supplement with ketamine only @ 1/3 dose
Ketamine + Medetomidine	75 mg/kg (K) + 0.5 mg/kg (M) IP or SC	
Urethane	1000 – 1500 mg/kg IP	Caution! Prolonged anesthesia; terminal procedures only; carcinogenic and mutagenic
Inactin	80 – 100 mg/kg IP	
Tiletamine - Zolazepam (Telazole®)	20 – 40 mg/kg IP	Concentration of reconstituted mixture is 100 mg/ml
Methohexital	40 mg/kg IP (1% solution)	20 minutes of anesthesia
Equithesin	3 ml/kg IP	40 minutes of anesthesia; fresh mixture required
Analgesia in Rats		
Morphine	10 mg/kg SC	Up to 3 hours of analgesia
Meperidine	20 mg/kg SC	Up to 3 hours of analgesia
Imipramine	10 mg/kg SC	Up to 12 hours of analgesia
Butorphanol (Torbutrol® 0.5mg/ml)	0.05 – 2.0 mg/kg SC	1 – 2 hours of analgesia
Buprenorpine (Buprenex®)	0.01 – 0.5 mg/kg SC	From 6 – 8 hours of analgesia
Ketoprofen	5.0 mg/kg SC	From 12 - 24 hours of analgesia
Carprofen	5.0 mg/kg SC	From 12 - 24 hours of analgesia
Sedation in Rats		
Medetomidine	30 – 100 µg/kg SC	Reverse with Atipamezole @ 1.0 µg/kg SC, IP, or IV
Ketamine	50 – 100 mg/kg IP	

Note: Rats have a relatively small total muscle mass and are prone to develop muscular atrophy or nerve damage following IM injections. The IM route should be used with caution in rats. If drugs must be administered via the IM route, minimal injection volumes (≤0.3 ml), and a 25-gauge needle or smaller should be used.

Table IV. Anesthetics and Analgesics used in Hamsters

Anesthesia in Hamsters	Dose & Route	Comments
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	70 – 90 mg/kg IP	Caution! Potentially significant cardiovascular and respiratory depression, variable response
Ketamine+Xylazine	80 – 100 mg/kg (K) + 7 – 10 mg/kg (X) IP	
Ketamine + Medetomidine	100 mg/kg (K) + 0.25 mg/kg (M) IP	
Tiletamine - Zolazepam (Telazole®)	20 – 40 mg/kg IP for sedation 50 – 80 mg/kg IP for anesthesia	
Telazole® + Xylazine	30 mg/kg (T) + 10 mg/kg (X) IP	
Urethane	1500 mg/kg IP	Caution! Prolonged anesthesia; terminal procedures only; carcinogenic and mutagenic
Urethane (50%) + α-Chloralose (10%) + Pentobarbital	380 mg/kg (U) + 38 mg/kg (C) + 26 mg/kg (P) IP	Anesthesia extended with 135 mg (U) + 14 mg (C) IP
Analgesia in Hamsters		
Morphine	10 mg/kg SC	Up to 3 hours of analgesia
Meperidine	20 mg/kg SC	Up to 3 hours of analgesia
Buprenorpnine (Buprenex®)	0.05 – 0.5 mg/kg SC	Between 8 – 12 hours of analgesia
Sedation in Hamsters		
Chlorpromazine	0.5 mg/kg IM	
Ketamine	40 - 80 mg/kg IP	

Table V. Anesthetics and Analgesics used in Guinea Pigs

Anesthesia in Guinea Pigs	**Dose & Route**	**Comments**
Isoflurane (Forane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer required, scavenging required
Ketamine + Xylazine	40 mg/kg (K) + 5 mg/kg (X) IP	Up to 60 minutes of anesthesia
Ketamine + Diazepam	100 mg/kg (K) + 5 mg/kg (D) IM	Up to 45 minutes of anesthesia
Ketamine + Acepromazine	125 mg/kg (K) + 5 mg/kg (A) IP	Up to 120 minutes of anesthesia
Ketamine + Medetomidine	40 mg/kg (K) IP, IM + 0.5 mg/kg (M) SC	Up to 40 minutes of anesthesia
Fentanyl/Fluanisone (Hypnorm®) + Diazepam	1.0 ml/kg (F/F) + 2.5 mg/kg (D) IM, IP	Up to 60 minutes of anesthesia
Pentobarbital	37 mg/kg IP	Up to 90 minutes of anesthesia Caution! Potentially significant cardiovascular and respiratory depression, variable response
A-Chloralose (1%) + Urethane (40%) in a 7:1 mixture	8.0 ml/kg IP	Approximately 2 hours of anesthesia
Analgesia in Guinea Pigs		
Carprofen (Rimadyl®)	4 mg/kg SC	Up to 24 hours of analgesia
Ketoprofen	1 mg/kg SC, IM	Up to 24 hours of analgesia
Morphine	2-5 mg/kg, SC, IM	Up to 4 hours of analgesia
Meperidine	10-20 mg/kg IM, SC	Up to 3 hours of analgesia
Buprenorphine (Buprenex®)	0.05 mg/kg SC	Up to 12 hours of analgesia
Sedation in Guinea Pigs		
Acepromazine	0.5-1.0 mg/kg IM, 2.5 – 5 mg/kg IP	Light to moderate sedation
Diazepam	2.5 – 5.0 mg/kg IP, IM	Moderate to heavy sedation
Ketamine	22 - 44 mg/kg IM	Light to heavy sedation
Midazolam	1.0 – 5.0 mg/kg IM, IP	Heavy sedation

Note: Guinea pigs often have a large amount of pasty feed in their mouths that can cause airway obstruction when anesthetized. This residue can be removed by gently rinsing the mouth with water before induction of anesthesia. IM injections of ketamine may result in self-mutilation and muscle necrosis. Anticholinergic medication (e.g., atropine @ 0.05 mg/kg SC or glycopyrrolate @ 0.01-0.02 mg/kg SC) may be used to reduce bronchial secretions and salivation. Normal values: body temperature 37.2-39.5ºC (99-103.1ºF); heart rate 230-380/min; respiration rate 40-100/min.

Table VI. Anesthetics and Analgesics used in Rabbits

Anesthesia in Rabbits	**Dose & Route**	**COMMENTS**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	30 – 40 mg/kg IV	Caution! Potentially significant cardiovascular and respiratory depression, variable response
Ketamine + Xylazine	35 – 50 mg/kg (K) + 5 – 10 mg/kg (X) IM	Minor procedures; up to 45 minutes of anesthesia; can supplement with ketamine @ 1/3 dose
Ketamine + Medetomidine	25 mg/kg (K) + 0.5 mg/kg (M) IM	
α-Chloralose	80 – 100 mg/kg IV	
Urethane	1000 mg/kg IV or IP	Caution! Prolonged anesthesia; terminal procedures only; carcinogenic and mutagenic
Equithesin	1 – 3 ml/kg	Fresh solutions only
Analgesia in Rabbits		
Morphine	2 – 5 mg/kg SC	Up to 3 hours of analgesia
Meperidine	10 mg/kg SC	Up to 3 hours of analgesia
Butorphanol (Torbutrol® 0.5mg/ml)	0.1 – 0.5 mg/kg SC, IM or IV	Up to 4 hours of analgesia
Buprenorpnine (Buprenex®)	0.01-0.05 mg/kg SC	Between 6 – 12 hours of analgesia
Carprofen	1.5 mg/kg SC	Between 12 – 24 hours of analgesia
Ketoprofen	1.0 mg/kg SC or IM	Up to 24 hours of analgesia
Sedation in Rabbits		
Butorphanol + Acepromazine	1 mg/kg (B) + 1 mg/kg (A) IM	
Chlorpromazine	25 – 100 mg/kg IM	
Acepromazine	0.75 – 1.0 mg/kg IM	
Diazepam	5 – 10 mg/kg IM	
Ketamine	30 mg/kg IM	
Xylazine	3 – 5 mg/kg IM or SC	

Note: Anesthetic depth: Adequate anesthesia for surgery can be very difficult to obtain in rabbits, especially when barbiturates are used. Rabbits are prone to develop respiratory depression and edema when anesthetized. Atropinase: Although atropine is frequently administered to anesthetized animals to reduce oral and respiratory secretions and to support heart rate, many rabbits (up to 50%) have circulating atropinase and thus may demonstrate a reduced duration of effectiveness of this drug. Normal values: body temperature 38.5-39.0°C (101.3-102.2°F); heart rate 130-300/min; respiration rate 30-60/min.

Table VII. Anesthetics and Analgesics used in Dogs

Anesthesia in Dogs	**Dose & Route**	**Comments**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	20 – 30 mg/kg IV	Caution! Divide dose and administer ½ as bolus and ½ to effect; between 30 – 45 minutes of anesthesia
Thiopental	8 – 12 mg/kg IV	Short acting, up to 15 minutes of anesthesia
Chloralose	80 – 110 mg/kg IV	Between 6 – 10 hours of anesthesia, premedicate with morphine @ 5 mg/kg, terminal procedures
Ketamine + Diazepam	10 mg/kg (K) + 0.5 mg/kg (D) IV (anesthesia for minor procedures) 5.5 mg/kg (K) + 0.3 mg/kg (D) IV (induction of anesthesia)	Premedicate with an anticholinergic Anesthesia can be maintained with inhalant anesthetic (e.g., isoflurane)
Ketamine + Midazolam	10 mg/kg (K) + 0.5 mg/kg (M) IV	Minor procedures; premedicate with anticholinergic
Telazole® (Tiletamine + Zolazepam)	6 – 8 mg/kg IM	Up to 1 hour of anesthesia
Telazole® + Xylazine + Butorphanol	6 – 8 mg/kg (T) + 0.5 mg/kg (X) + 0.2 mg/kg (B) IM	
Analgesia in Dogs		
Meperidine	2 – 10 mg/kg SC or IM	Up to 3 hours of analgesia
Morphine	0.25 – 5.0 mg/kg IM or SC	Between 4 – 6 hours of analgesia
Butorphanol (Torbutrol® 0.5 mg/ml)	0.2 – 0.4 mg/kg IM or SC	Between 2 – 5 hours of analgesia
Buprenorpnine (Buprenex®)	0.01 – 0.02 mg/kg SC	Between 8 – 12 hours of analgesia
Carprofen	2.2 mg/kg PO, or 5 mg/kg SC	Up to 12 hours of analgesia
Ketoprofen	2 mg/kg SC or IM	Up to 24 hours of analgesia
Fentanyl patch	<5 kg body weight = ½ of 25 µg/hr patch; 5 – 10 kg bdy wt = 25 µg/hr patch; 10 – 20 kg bdy wt = 50 µg/hr patch; 20 – 30 kg bdy wt = 75 µg/hr patch; > 30 kg bdy wt = 100 µg/hr patch	Each dose provides up to 72 hours of analgesia; place 12 hours prior to anticipated pain; do not apply heat to patch (e.g., from heating pads).
Sedation in Dogs		
Butorphanol + Acepromazine	0.2 – 0.4 mg/kg (B) + 0.02 – 0.05 mg/kg (A) SC, IM, IV	
Buprenorphine + Acepromazine	0.007 mg/kg (B) + 0.03 – 0.05 mg/kg (A) SC, IM	
Xylazine	0.5 – 1.0 mg/kg IM	
Chlorpromazine	1 – 6 mg/kg IM, SC	
Acepromazine	0.05 – 0.1 mg/kg IM, SC	Maximum administer ≤3 mg total

Note: Anticholinergic medication (e.g., atropine @ 0.02-0.04 mg/kg SC, IM, or glycopyrrolate @ 0.02 mg/kg IM, SC) may be helpful in anesthetized dogs to support the heart rate and reduce bronchial secretions, consult a USF veterinarian.
Normal values: body temperature 37.5-39°C (99.5-102.2°F); heart rate 70-120/min, respiratory rate 15-25/min.

Table VIII. Anesthetics and Analgesics used in Cats

Anesthesia in Cats	Dose & Route	Comments
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Pentobarbital	20 – 30 mg/kg IV	Caution! Divide dose and administer ½ as bolus and ½ to effect; between 30 – 45 minutes of anesthesia
Ketamine + Diazepam	10 mg/kg (K) + 0.5 mg/kg (D) IV (anesthesia for minor procedures) 5.5 mg/kg (K) + 0.3 mg/kg (D) IV (induction of anesthesia)	Premedicate with an anticholinergic Anesthesia can be maintained with inhalant anesthetic (e.g., isoflurane)
Ketamine + Medetomidine	7.0 mg/kg (K) + 0.08 mg/kg (M) IM	Minor procedures; up to 45 minutes anesthesia
Analgesia in Cats		
Morphine	0.1 mg/kg IM or SC	Up to 4 hours analgesia; caution, mania and excitation with overdose
Meperidine	2 – 10 mg/kg IM or SC	
Buprenorpnine (Buprenex®)	0.005 – 0.01 mg/kg SC or IM	Up to 12 hours analgesia
Oxymorphone	0.05 – 0.15 mg/kg IM, SC or IV	Between 3 – 5 hours analgesia; Minimal respiratory depression
Carprofen	4.0 mg/kg SC or IV	Up to 24 hours analgesia
Ketoprofen	1.0 mg/kg SC, IM or IV	Up to 24 hours analgesia
Fentanyl patch	<2.5 kg body weight = ½ of 25 µg/hr patch; >2.5 kg bdy wt = 25 µg/hr patch	Each up to 5 days analgesia; place 8 hours prior to anticipated pain; do not apply heat to patch (e.g., from heating pads)
Sedation in Cats		
Butorphanol + Acepromazine	0.1 – 0.4 mg/kg (B) SC, IM or IV + 0.02 – 0.05 mg/kg (A) SC, IM or IV	
Ketamine	10 – 20 mg/kg (K) IM	
Acepromazine	0.05 – 0.1 mg/kg IM or SC	
Chlorpromazine	1.0 – 2.0 mg/kg IM	
Midazolam	0.2 – 0.4 mg/kg IV or IM	
Diazepam	0.2 – 0.4 mg/kg IV or IM	
Xylazine	0.4 – 0.9 mg/kg SC or IM	

Note: Acetaminophen (Tylenol) may be toxic in cats and should be used with extreme caution in this species. Cats are also sensitive to the toxic effects of aspirin, and fatalities have been reported. Although aspirin can be used in cats, other agents should be considered. Normal values: body temperature 38.0-39.5°C (100.4-103.1°F); heart rate 110-140/min; respiration rate, 20-30/min. Anticholinergic medication (e.g., atropine @ 0.02-0.04 mg/kg SC, IM, or glycopyrrolate @ 0.02 mg/kg IM, SC) may be helpful in anesthetized cats to support the heart rate and reduce bronchial secretions, consult a USF veterinarian.

Table IX. Anesthetics and Analgesics used in Pigs

Anesthesia in Pigs	Dose & Route	Comments
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Ketamine + Xylazine	20 mg/kg (K) + 2 mg/kg (X) IM	Up to 20 minutes of anesthesia; for minor procedures
Ketamine + Acepromazine	33 mg/kg (K) + 1.1 mg/kg (A) IM	
Pentobarbital	5 – 15 mg/kg IV	Administer to effect
Ketamine + Telazole®	2.2 mg/kg (K) + 4.4 mg/kg (T) IM	Up to 30 minutes of anesthesia
Telazole® + Xylazine	2.0 - 8.8 mg/kg (T) + 2.2 mg/kg (X) IM	Up to 20 minutes of anesthesia; may produce cardiopulmonary depression
Ketamine + Telazole® + Xylazine	2.2 mg/kg (K) + 4.4 mg/kg (T) + 2.2mg/kg (X) IM	Up to 30 minutes of anesthesia; for minor procedures
Ketamine + Medetomidine	10 mg/kg (K) + 0.08 mg/kg (M) IM	Immobilization; light anesthesia
Analgesia in Pigs		
Aspirin	10 mg/kg PO	Up to 6 hours of analgesia; use enteric-coated tablet
Meperidine	4 – 10 mg/kg IM	Up to 4 hours of analgesia
Phenylbutazone	10 – 20 mg/kg PO	Up to 12 hours of analgesia; use to alleviate musculoskeletal pain
Buprenorpnine (Buprenex®)	0.005 - 0.01 mg/kg IM	Up to 12 hours of analgesia
Ketoprofen	1.0 – 3.0 mg/kg SC	Up to 24 hours of analgesia
Carprofen	0.5 - 4.0 mg/kg SC	Up to 24 hours of analgesia
Sedation in Pigs		
Acepromazine	0.11 – 1.1 mg/kg SC or IM	
Chlorpromazine	0.5 – 4.0 mg/kg IM or SC	
Diazepam	0.5 – 10 mg/kg IM	Usually combined w/other agents
Azaperone (Stresnil®)	2 – 8 mg/kg IM	

Note: Malignant hyperthermia (MH) is commonly reported in swine. The first cardinal clinical sign of MH is an elevation in end-tidal CO_2. MH is characterized by the sudden onset of muscle rigidity, tachypnea, tachycardia and hyperthermia (rectal temperatures up to 108°F), followed by dyspnea, cardiac arrhythmias, apnea and death. Anesthesia (particularly with halothane, isoflurane, or ethrane), restraint, stress and excitement have all been reported to trigger this condition. Anesthetized swine should be monitored closely for the development of hyperthermia. Emergency measures include cessation of the anesthetic, cooling the body with ice water, and the IV administration of sodium bicarbonate and the muscle relaxant dantrolene (2-10 mg/kg). Normal values: temperature 38.0-40.0°C (100.4-104.0°F); heart rate 60-120/min; respiration rate 10-12/min. Anticholinergic: Glycopyrrolate (0.004-0.01 mg/kg IM) or atropine (0.05 mg/kg IM).

Table X. Anesthetics and Analgesics used in Sheep and Goats

Anesthesia in Sheep & Goats	Dose & Route	Comments
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate ventilation or scavenging essential
Diazepam + Ketamine	0.1 mg/kg (D) + 4.5 mg/kg (K) IV	Up to 20 minutes of anesthesia; for minor procedures
Xylazine + Ketamine (Goat) (Sheep) (Goat) (Sheep)	0.05 mg/kg (X) + 4-5 mg/kg (K) IV 0.2 mg/kg (X) + 4-5 mg/kg (K) IV 0.1 mg/kg (X) + 10-15 mg/kg (K) IM 0.2 mg/kg (X) + 10-15 mg/kg (K) IM	Up to 20 minutes of anesthesia; for minor procedures Up to 45 minutes of anesthesia
Pentobarbital	20-30 mg/kg IV	Administer to effect
Telazole®	2-4 mg/kg IV	Up to 30 minutes of anesthesia
Xylazine + Telazole®	0.1 mg/kg (X) + 4 mg/kg (T) IM 0.05 mg/kg (X) + 1 mg/kg (T) IV	Up to 60 minutes of anesthesia
Ketamine + Medetomidine	0.5-1 mg/kg (K) + 20-25 µg/kg (M) IM	Up to 60 minutes of anesthesia
Analgesia in Sheep & Goats		
Aspirin	50-100 mg/kg PO	Up to 12 hours of analgesia
Flunixin	1-2 mg/kg IV, IM	Up to 24 hours of analgesia; only administer post-operatively to conscious animals
Meperidine	2 mg/kg IM, IV	Up to 4 hours of analgesia
Butorphanol + Diazepam	0.05-0.1mg/kg (B) + 0.05-0.2 mg/kg (D) IV	Up to 4 hours of analgesia
Buprenorphine (Buprenex®)	0.005-0.01 mg/kg IM	Up to 4 hours of analgesia
Sedation in Sheep & Goats		
Acepromazine	0.05-0.1 mg/kg IM, SC	Moderate sedation
Diazepam	0.2-0.5 mg/kg IV, IM	Light sedation
Ketamine	20 mg/kg IM	Moderate to heavy sedation
Medetomidine	25 µg/kg IM	Light to heavy sedation
Xylazine	0.2 mg/kg IV, IM (Sheep) 0.05 mg/kg IV, IM (Goat)	Light to moderate sedation

Note: Medetomidine and Xylazine can produce hypoxia. Goats and sheep may be fasted for 24-36 hours to reduce the possibility of regurgitation and ruminal tympany (bloat). Water may be withheld 6-8 hours. Always intubate with a cuffed endotracheal tube to prevent aspiration if regurgitation occurs. Intraoperatively a stomach tube should always be placed in the rumen to prevent ruminal tympany, especially when positioned in lateral or dorsal recumbency. Normal values: temperature 38.0-40°C (100.4-104.0°F); heart rate 55-120/min (Sheep), 70-130 (Goat); respiration rate 10-30/min. Anticholinergic drugs are not routinely used during ruminant surgery, but are beneficial in treating bradycardia: glycopyrrolate (0.022 mg/kg IM, SC) or atropine (0.05 mg/kg IM, SC).

Table XI. Anesthetics and Analgesics used in *Macaca* spp

Anesthesia in *Macaca* spp	**Dose & Route**	**Comments**
Isoflurane (Forane®) Halothane (Fluothane®) Enflurane (Ethrane®)	To effect. In general, 3-4% induction, 1-2% maintenance; inhalation	Precision vaporizer, adequate scavenging essential
Ketamine + Diazepam	15 mg/kg (K) + 1.0 mg/kg (D) IM	30-40 minutes of anesthesia
Ketamine + Xylazine	10 mg/kg (K) + 0.25-2.0 mg/kg (X) IM	30-140 minutes of anesthesia; duration is a function of the xylazine dose
Ketamine + Medetomidine	2-6 mg/kg (K) + 30-60 µg/kg (M) IM	Up to 60 minutes of anesthesia
Pentobarbital	20-30 mg/kg IV	30-60 minutes of anesthesia: reduce dose by $^{1}/_{3}$ to $^{1}/_{2}$ after administration of ketamine
Thiopental	15-20 mg/kg IV 5-7 mg/kg IV (induction)	5-10 minutes of anesthesia After administration of ketamine
Telazole®	4-6 mg/kg IM	45-60 minutes of anesthesia
Analgesia in *Macaca* spp		
Acetaminophen	10 mg/kg PO	Up to 6 hours of analgesia
Aspirin	20mg/kg PO 125 mg/kg rectal suppository	6 to 8 hours < 24 hours
Ketoprofen	5 mg/kg IM	Up to 8 hours of analgesia
Carprofen	2-4 mg/kg PO, SC	Up to 24 hours of analgesia
Ketorolac	15-30 mg/kg IM	
Flunixin	2-4 mg/kg, SC	Up to 24 hours of analgesia; only administer postoperatively to conscious animals
Meloxicam	0.1-0.3 mg/kg PO	Up to 24 hours of analgesia
Naproxen	10 mg/kg PO	Up to 12 hours of analgesia
Oxymorphone	0.15 mg/kg SC, IM, IV	Up to 6 hours of analgesia
Meperidine	2-4 mg/kg IM	Up to 4 hours of analgesia
Morphine	1-2 mg/kg SC, IM	Up to 4 hours of analgesia
Buprenorphine (Buprenex®)	0.005-0.01 mg/kg IM	Up to 8 hours of analgesia
Sedation in *Macaca* spp		
Acepromazine	0.2 mg/kg IM	Moderate sedation
Diazepam	1.0 mg/kg IM	Light to moderate sedation
Ketamine	5-20 mg/kg IM	Moderate sedation, immobilization
Xylazine	0.25-0.5 mg/kg IM	Light to moderate sedation

Note: Anticholinergics: Medetomidine and Xylazine can produce bradycardia and hypotension, in particular at the high end of the xylazine dose. These side effects can be prevented by pre-medicating with atropine (0.02-0.05 mg/kg IM) or glycopyrrolate (0.005-0.01 IM). Anticholinergics also reduce bronchial and salivary secretions. Food: Nonhuman primates should be fasted for at least 12 hours prior to elective surgery. Normal Values: temperature 37-39° C (98.6-103.1° F); heart rate 120-180/min; respiration rate 32-50/min.