## Local Anaesthetics

## analgesic drugs

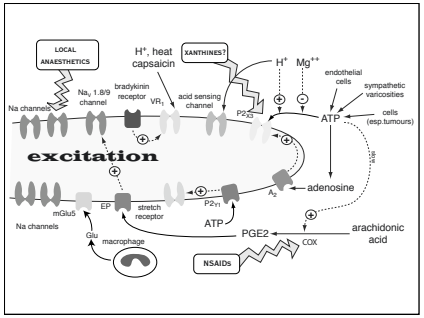
- opioids
- NSAIDs
- α2 agonists
- local anaesthetics
- others

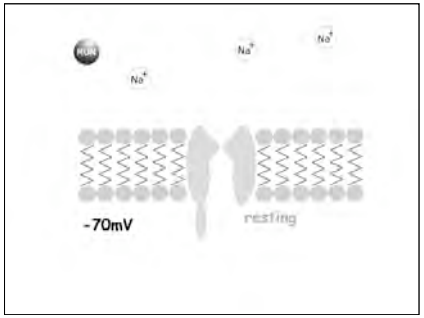
## anaesthesia

- general
- local
- regional

## definitions

- anaesthesia = loss of feeling
- analgesia = loss of pain
- local anaesthesia = local analgesia




## Na channel subtypes

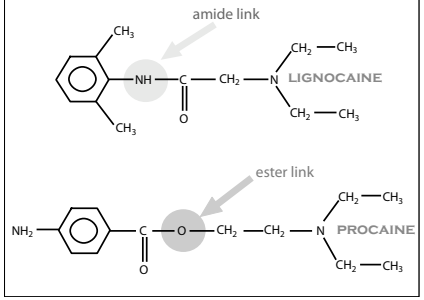
- **CNS $Na_V1.1$, 1.2, 1.3**
- **skeletal muscle $Na_V1.4$**
- **heart $Na_V1.5$**
- **dorsal root ganglia $Na_V1.8$,1.9**
- **neurendocrine & peripheral neurones $Na_V1.7$**
- **all neurones & glia $Na_V1.6$**

## Na channel blockers

- **local anaesthetics**
- **class 1 antiarrhythmics**
- **some anticonvulsants**

## chemistry

- lipophilic end
- hydrophilic end
- amide or ester link in middle
- nb many drugs have this sort of structure

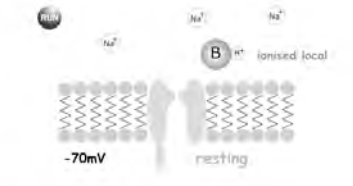



## chemistry

- most are weak bases
- most have $pK_a$ 8 – 9

## drug access to channels

- via membrane
  - drug must be unionised
- via channel
  - channel must be open




## use dependence

- the more the nerve fires,
- the more channels are open,
- the more easily the drug gets in,
- the faster it works
- drugs also bind best to inactivated channels

## “incomplete” block

- low doses reduce frequency of firing
- useful for
  - arrhythmias
  - convulsions
  - neuropathic pain
    - horses?

## differential block

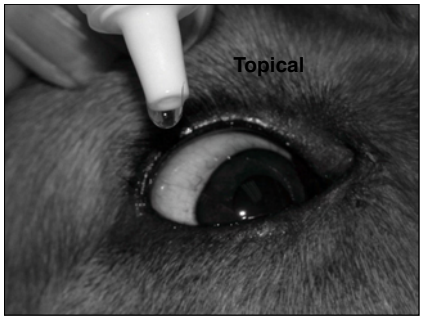
- small fibres blocked faster than big ones
- pain signals carried by small fibres
- pain should be blocked first
- doesn’t work very well in real life

## indications for local anaesthetics

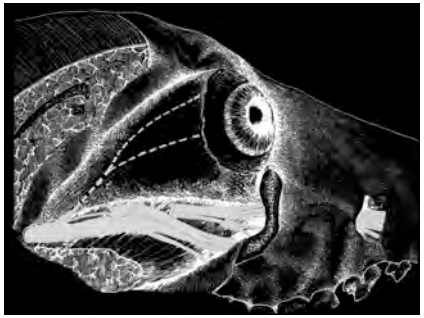
- operative analgesia
- postoperative analgesia
- diagnosing lameness
- (arrhythmias)

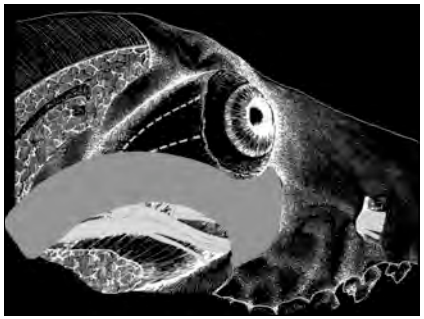
## administration

- topical
- local infiltration
- nerve block
- epidural / intrathecal
- Bier's block (IVRA)
- intra-articular
- (iv)




## local infiltration



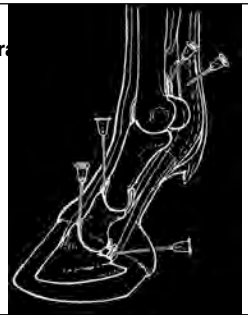


## Epidural / Intrathecal

- **Contraindications**
  - **History of Trauma**
  - **Deformity**
  - **Systemic or Local Infection**
  - **Hypovolaemia**
  - **Clotting Disorder**
  - **Blood / CSF Aspiration**

ock)

Intra

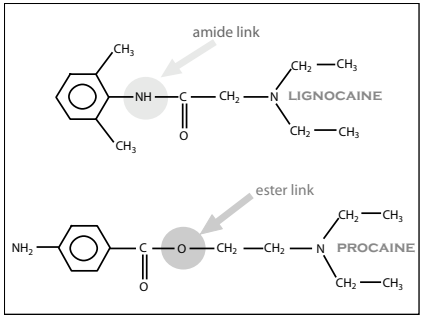


## intravenous

- has been used in people & horses
- does it work??

## pharmacokinetics

- injected somewhere near nerve
- penetrate nerve fibres
- diffuse out of nerve
- distributed away by blood
  - vasoconstrictors
- metabolised
- metabolites eliminated

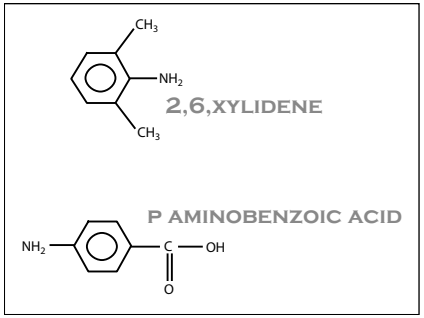



## esters

- **hydrolysis by non-specific esterases**
- **plasma and liver**
- **fast**

## amides

- **N dealkylation**
- **liver**
- **slower but still fairly fast**



## side effects

- convulsions
- sedation
- respiratory depression
- reduced cardiac output
- vasodilatation

## toxicity

- overdose
  - sheep
- accidental iv injection

## common drug

- lignocaine (= lidocaine)
  - 2% solution pH5.6, pKa7.7
  - onset of action about 2mins
  - lasts 20 – 40 mins
  - very stable – can be autoclaved

## less common drugs

- prilocaine
- mepivacaine
- bupivacaine

## rarely used drugs

- amethocaine (= tetracaine)
- proxymethacaine
- cinchocaine (= dibucaine)
- ropivacaine
- benzocaine

## toxins

- tetrodotoxin
- saxitoxin

## channel openers

- DDT and pyrethrum
- veratridine
- some spider and scorpion toxins

## local anaesthetics

- stop action potentials by blocking sodium channels
- are weak bases which get into cells in the unionised form, become ionised and bind to the channels in the open or inactivated state.
- show use dependence – rate of onset and depth of block are dependent on action potential frequency
- block pain fibres before motor fibres
- are mainly used for analgesia – particularly in ruminants
- block most excitable tissues if you give too much