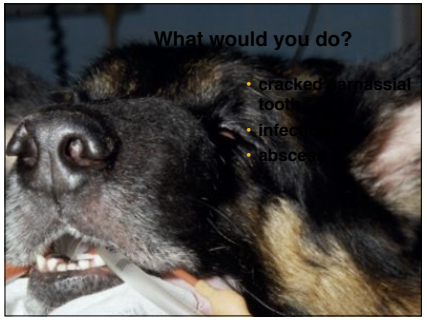
Local Anaesthetics

by the end of this lecture you should be able to

- formulate an analgesic plan using local anaesthetics
- know when a different approach would be better



analgesic drugs

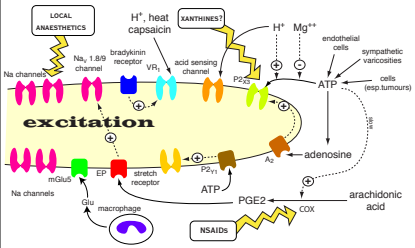
- opioids
- NSAIDs
- α2 agonists
- local anaesthetics
- others

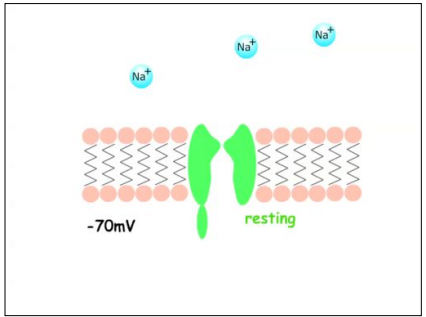
anaesthesia

- general
- local
- regional

definitions

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





Na channel subtypes

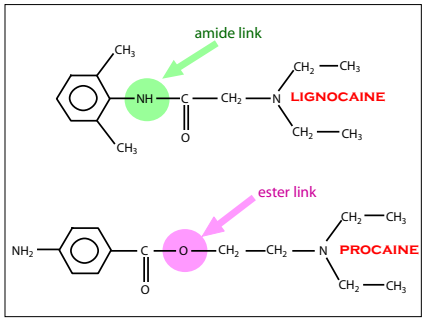
- CNS $Na_V1.1$, 1.2, 1.3
- skeletal muscle $Na_V1.4$
- heart $Na_V1.5$
- dorsal root ganglia $Na_V1.8$,1.9
- neurendocrine & peripheral neurones $Na_V1.7$
- all neurones & glia $Na_V1.6$

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

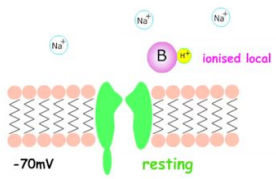


chemistry

- 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

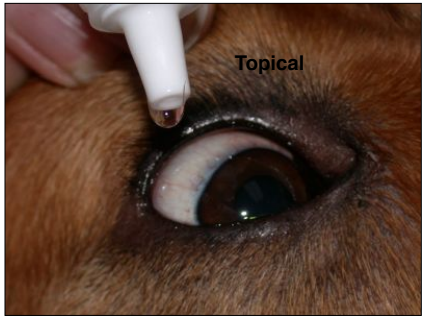
- small fibres blocked faster than big ones
- pain signals carried by small fibres
- pain should be blocked first
- doesn’t work very well in real life

indications for local anaesthetics

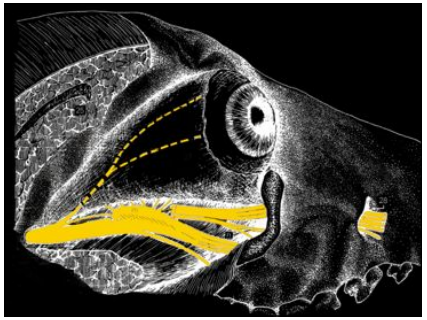
- operative analgesia
- postoperative analgesia
- diagnosing lameness
- (arrhythmias)

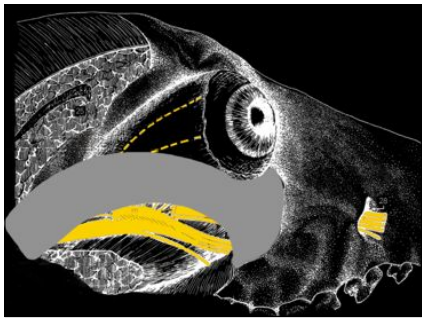
administration

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


Topical

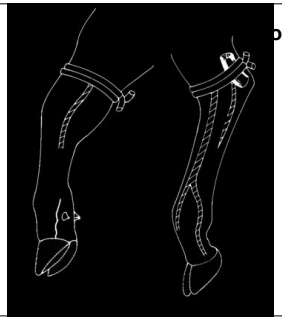

al infiltration





Epidural / Intrathecal

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



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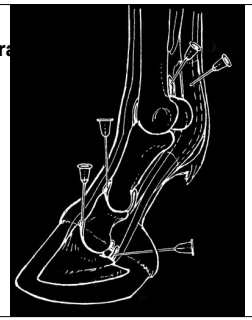


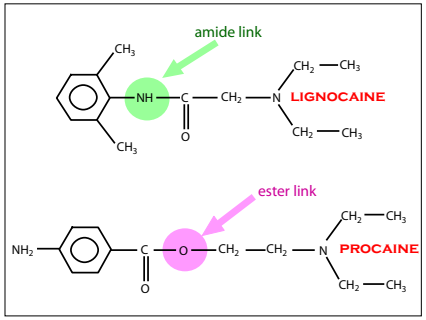
Intra

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

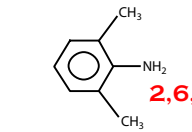


esters

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

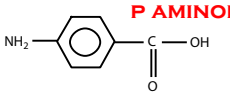
amides

- N dealkylation
- liver
- slower but still fairly fast



2,6,XYLIDENE

P AMINOBENZOIC ACID



side effects

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

toxicity

- overdose
  - sheep
- accidental iv injection

common drug

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

less common drugs

- prilocaine
- mepivacaine
- bupivacaine

rarely used drugs

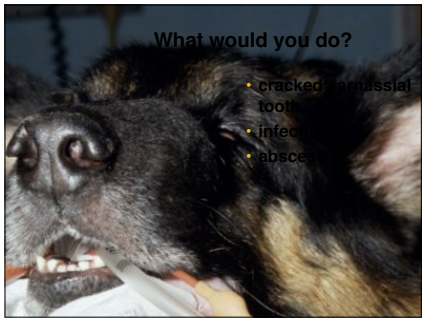
- amethocaine (= tetracaine)
- proxymethacaine
- cinchocaine (= dibucaine)
- ropivacaine
- benzocaine

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
- are usually given around a nerve
- block pain fibres before motor fibres
- are mainly used for analgesia - particularly in ruminants
- block most excitable tissues if you give too much