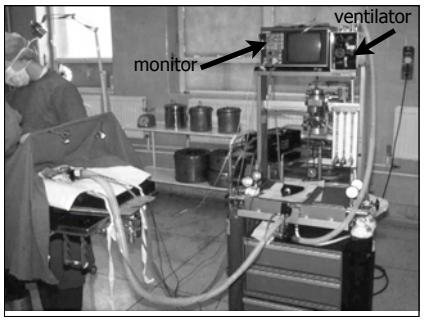
Neuromuscular Junction

NMJ

- muscle relaxation during anaesthesia
- myaesthenia gravis
- poisoning

balanced anaesthesia

- unconsciousness
- analgesia
- muscle relaxation



neuromuscular blockers

- depolarising (non competitive)
- competitive (non depolarising)
- (inhibition of ACh synthesis)
- (inhibition of ACh release)
  - magnesium
  - aminoglycoside antibiotics
  - botulinum toxin

neuromuscular blockers stop the animal's breathing and cause paralysis – the animal

must

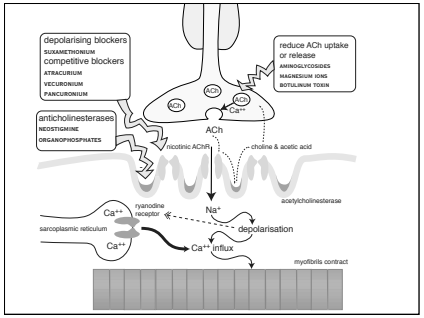
be unconscious before they are used

anaesthesia

- given iv after anaesthetic
- ventilation required
- degree of blockade monitored

onset of blockade

- 1 tail & face
- 2 limbs
- 3 swallowing
- 4 abdominal muscles
- 5 intercostal muscles
- 6 diaphragm



suxamethonium

- **succinylcholine USAN**
- **depolarising blocker**
- **acts like ACh**
- **2 ACh molecules joined**
- **hydrolysed by plasma cholinesterase**
- **succinylcholine USAN**

suxamethonium

- **depolarises muscle fibre**
- **fasiculation**
- **effects not reversible**

side effects

- **potassium release**
- **bradycardia**
- **muscle pain later?**
- **can provoke malignant hyperthermia in pigs**

phase 2 block

- prolonged blockade after several doses of suxamethonium
- competitive
- partially reversible
- receptor desensitisation?

sux indications

- muscle relaxation for intubation (crash induction)
- (relaxation for caesarian section)

sux contra-indications

- no means of ventilation available
- doubt about unconsciousness
- recent OP administration

sux pharmacokinetics

- acts in one circulation time
- diffuses out of synapse
- metabolised by plasma cholinesterases
- effects wear off in 2 – 3 mins
  - dogs 20 mins
- anticholinesterases prolong effects
  - organophosphate insecticides

competitive blockers

- compete with ACh for receptor
- effect reversed by increasing ACh concentration

competitive blockers

- actions influenced by other drugs
  - inhalation anaesthetics
  - benzodiazepines
  - aminoglycoside antibiotics

competitive blockers

- atracurium
- vecuronium
- pancuronium
- mivacurium
- rocuronium

atracurium

- acts for about 20 – 30 mins
- broken down by Hofmann degradation
  - liver function not necessary

vecuronium

- lasts 15 – 20 mins
- non cumulative
- metabolised in liver

pancuronium

- lasts 40 – 50 mins
- can cause tachycardia
- must be reversed

mivacurium

- rapid block – 2mins
- short action – 10 – 15 mins

rocuronium

- rapid onset – 1 min
- duration 30 – 40 mins

do not use

- no longer available in NZ
- tubocurare
  - causes histamine release
  - kills dogs
- pipecuronium
  - similar to pancuronium but longer acting & more side effects

indications

- muscle relaxation during anaesthesia
  - thoracotomy
  - ophthalmic ops
  - some abdominal ops
  - (reducing dislocations)

after use

- effects can be reversed with anticholinesterase
- anticholinesterase increases ACh which competes with blocker

anticholinesterases

- edrophonium
  - short acting, no longer available in NZ
- neostigmine
  - medium duration of action
- pyridostigmine
  - long acting, inj not available in NZ
- all must be given with atropine

myaesthenia gravis

- autoantibodies to nACh R (& thymus in man)
- muscle weakness, megoesophagus
- diagnosis – improvement with neostigmine (+ atropine)
- treatment – pyridostigmine po

others

- reduce ACh release
  - magnesium
  - streptomycin
  - botulinus toxin
- compete with Ca in muscle
  - magnesium

malignant hyperthermia

- defect in gene for ryanodine receptor
- common in pigs
- probably occurs in most species
- usually triggered by halothane
- can be triggered by suxamethonium

malignant hyperthermia

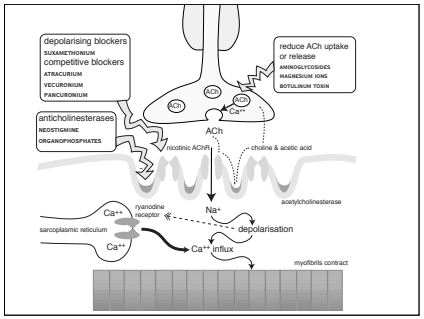
- pig goes rigid
- temperature goes up
- tachycardia then tachyarrhythmias
- cyanosis
- acidosis
- later
  - all the signs of muscle breakdown

MH treatment

- stop giving halothane
- ventilate with oxygen
- cool down
- give dantrolene

dantrolene

- does not act at NMJ
- prevents calcium release from sarcoplasmic reticulum
- uncouples excitation and contraction
- used in malignant hyperthermia
- too expensive to use



neuromuscular blockers

- neuromuscular blockers used for anaesthesia for some ops
- they must not be given to conscious animals
- animals must be ventilated
- do not use these drugs unless you have equipment for IPPV and know what you are doing