

## Adrenergic Transmission

### by the end of this lecture

- you should be able to formulate a treatment strategy for an animal with vasodilatation

What would you do?



### downer cow



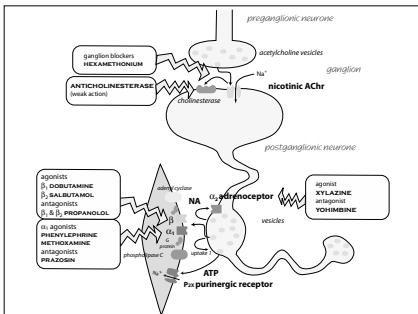
given dexamethasone  
10 mins earlier to induce  
calving  
now gone down  
some swelling around  
perineum  
shaking / muscle  
twitching  
grunting respiration

## adrenergic transmission

- noradrenaline (norepinephrine USAN)  
from sympathetic nerve endings
- adrenaline (epinephrine USAN)  
from adrenal glands
- (dopamine)  
mainly in CNS
- but also gut & visceral blood vessels

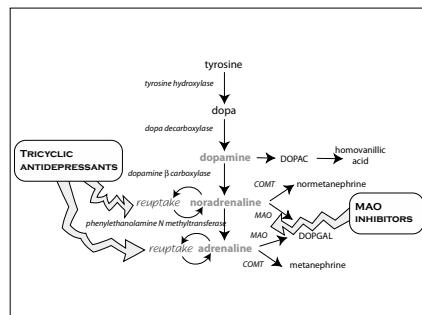
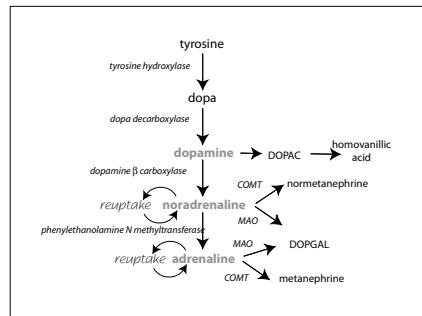
## sites of drug action

- synthesis
- storage
- release
- receptor binding
- uptake



## sites of drug action

- synthesis
- false transmitters
  - methyl dopa
  - 6 hydroxydopamine
- storage
- release
- receptor binding
- uptake



### sites of drug action

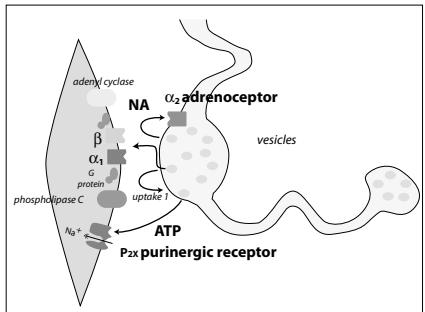
- synthesis
- storage
  - reserpine
    - blocks uptake into vesicles
    - causes NA depletion
- release
- receptor binding
- uptake

### sites of drug action

- synthesis
- storage
- release
  - guanethidine
  - bretlyium
  - Ca blockers
- receptor binding
- uptake

## sites of drug action

- synthesis
- storage
- release
- receptor binding
- uptake



receptor	transmitter	useful effects	agonist	antagonist
α1	adrenaline noradrenaline	vasoconstriction mydriasis	phenylephrine	prazosin
α2	adrenaline noradrenaline	(vasodilatation) sedation & analgesia	xylazine detomidine	yohimbine atipamezole
β1	adrenaline (noradrenaline)	+ve inotropy tachycardia	dobutamine dopamine	atenolol metoprolol
β2	adrenaline	bronchodilation vasodilatation (musc)	salbutamol clenbuterol	propranolol (nonselective)
(β3)	adrenaline	lipolysis	SRS8611A	SR59230A

## α<sub>2</sub> adrenoceptors

- presynaptic in periphery
- postsynaptic in CNS
- always inhibit the neurone they are on

### **clinical use of agonists**

- heart failure
  - adrenaline &  $\beta_1$  agonists
- anaphylactic reactions
  - adrenaline
- delay parturition
  - clenbuterol
- sedation and analgesia
  - xylazine and  $\alpha_2$  agonists

### **clinical use of antagonists**

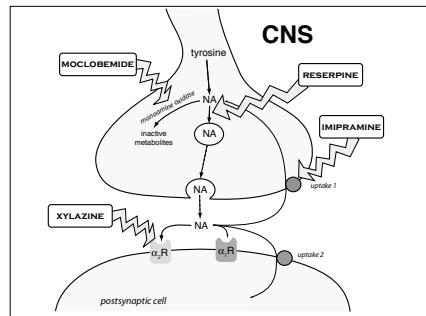
- slow heart
  - $\beta_1$  blockers
- (vasodilatation)
  - $\alpha_1$  blockers
- reversal of  $\alpha_2$  sedation
  - $\alpha_2$  blockers

### **sympathomimetics**

- directly acting
  - at receptors
- indirectly acting
  - alter NA release / uptake
  - usually have some direct effect as well
- mixed

### **sites of drug action**

- synthesis
- storage
- release
- receptor binding
- uptake



### uptake inhibitors

- used for CNS effects
- beware peripheral side effects

### uptake inhibitors

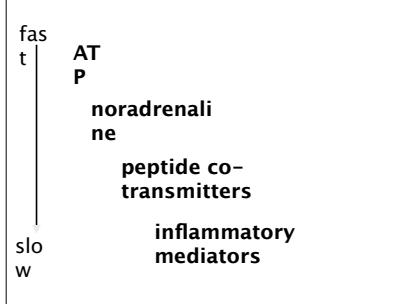
- tricyclic antidepressants
- "selective" serotonin uptake inhibitors (SSRIs)
- monoamine oxidase inhibitors
- (cocaine)
- (amphetamine)

### co-transmission

- vesicle released at synapse
- mixture of transmitters in vesicle
  - noradrenaline
  - ATP
  - neuropeptide Y (& in separate vesicles)
  - others???
- mixture may not always be the same

## co-transmission

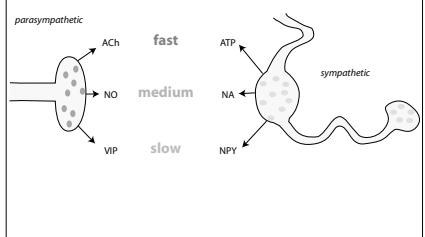
- ATP
  - P2x purinoceptors responsible for fast transmission
    - > 7 subtypes
    - CNS as well as smooth muscle & peripheral nerves
  - P2y purinoceptors ??
    - potentiates effects of noradrenaline
- peptides
  - neuropeptide Y
  - chromogranin??

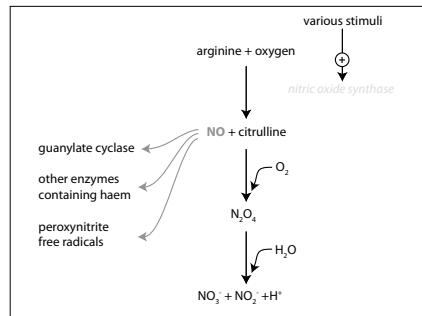


## non-adrenergic non-cholinergic transmission

- nitric oxide
- vasoactive intestinal peptide
- neuropeptide Y
- gonadotrophin releasing hormone
- 5 hydroxytryptamine
- $\gamma$  aminobutyric acid
- dopamine

## NANC transmission





### NANC transmission

- nitric oxide
  - relaxes smooth muscle
  - neuronal excitation
  - excitotoxicity

### oxides of nitrogen

- nitric oxide - NO
  - vasodilator & neuromodulator
- nitrous oxide - N<sub>2</sub>O
  - anaesthetic gas
- nitrogen dioxide - NO<sub>2</sub>
  - environmental pollutant
- do not mix them up!!!

### NANC transmission

- nitric oxide
  - nitrergic neurones
  - 2% of brain neurones



**downer cow**

given dexamethasone  
10 mins earlier to induce  
calving  
now gone down  
some swelling around  
perineum  
shaking / muscle  
twitching  
grunting respiration

**problems**

- histamine release
  - vasodilatation
  - increased vascular permeability
  - smooth muscle contraction
  - cardiac stimulation
  - increased abomasal secretions

**treatment?**

- adrenaline
  - route?
- antihistamines?

### (nor)adrenergic transmission

- NA synthesised from tyrosine & stored in vesicles
- release requires calcium
- NA binds to a variety of adrenergic receptors throughout the body
- action terminated by reuptake
- all these processes can be affected by drugs
- ATP co-transmission important