

**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



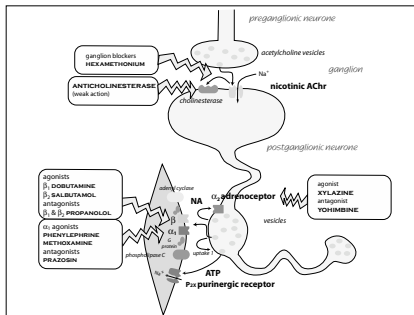
- given dexamethasone 10 mins earlier to induce calving
- now gone down
- some swelling around perineum
- shaking / muscle twitching
- grunting respiration

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

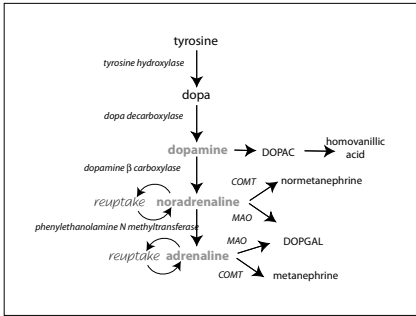
sites of drug action

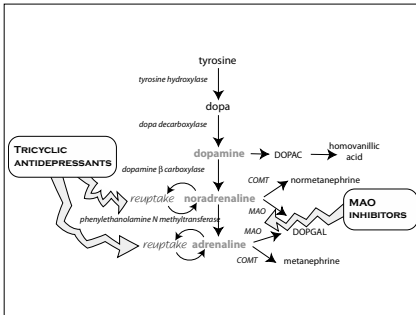
- synthesis
- storage
- release
- receptor binding
- uptake



sites of drug action

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





sites of drug action

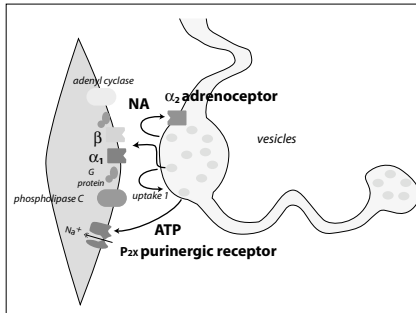
- synthesis
- storage
 - reserpine
 - blocks uptake into vesicles
 - causes NA depletion
- release
- receptor binding
- uptake

sites of drug action

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

sites of drug action

- synthesis
- storage
- release
- receptor binding
- uptake



receptor	transmitter	useful effects	agonist	antagonist
α_1	adrenaline noradrenaline	vasoconstriction mydriasis	phenylephrine	prazosin
α_2	adrenaline noradrenaline	(vasodilatation) sedation & analgesia	xylazine detomidine	yohimbine atipamezole
β_1	adrenaline (noradrenaline)	+ve inotropy tachycardia	dobutamine dopamine	atenolol metoprolol
β_2	adrenaline	bronchodilatation vasodilatation (muscle) uterine relaxation	salbutamol clenbuterol	propranolol (nonselective)
(β_3)	adrenaline	lipolysis	SR58611A	SR59230A

α_2 adrenoceptors

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

clinical use of agonists

- heart failure
 - adrenaline & β 1 agonists
- anaphylactic reactions
 - adrenaline
- delay parturition
 - clenbuterol
- sedation and analgesia
 - xylazine and α 2 agonists

clinical use of antagonists

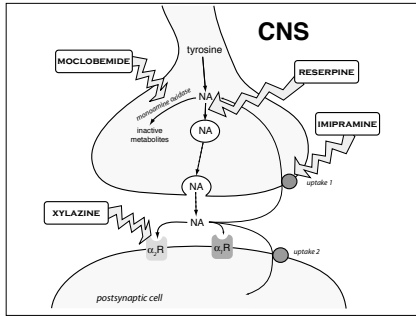
- slow heart
 - β 1 blockers
- (vasodilatation)
 - α 1 blockers
- reversal of α 2 sedation
 - α 2 blockers

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

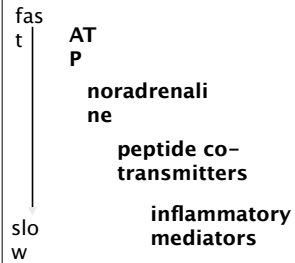
- tricyclic antidepressants
- "selective" serotonin uptake inhibitors (SSRIs)
- monoamine oxidase inhibitors
- (cocaine)
- (amphetamine)

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

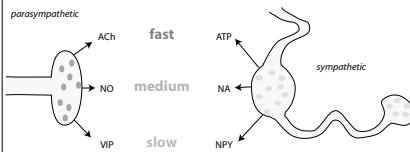
- ATP
 - P2x purinoceptors responsible for fast transmission
 - > 7 subtypes
 - CNS as well as smooth muscle & peripheral nerves
 - P2y purinoceptors ??
 - potentiates effects of noradrenaline
- peptides
 - neuropeptide Y
 - chromogranin??

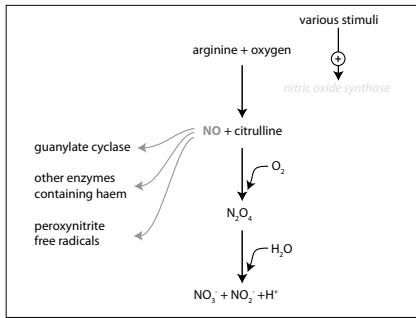


non-adrenergic non-cholinergic transmission

- nitric oxide
- vasoactive intestinal peptide
- neuropeptide Y
- gonadotrophin releasing hormone
- 5 hydroxytryptamine
- γ 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 - N₂O**
 - anaesthetic gas
- **nitrogen dioxide - NO₂**
 - environmental pollutant
- **do not mix them up!!!**

NANC transmission

- **nitric oxide**
 - nitrenergic neurones
 - 2% of brain neurones



downer cow



- given dexamethasone
- 10 mins ealier 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
