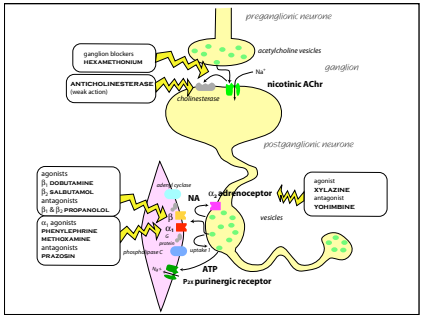
Adrenergic Transmission

adrenergic transmission

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

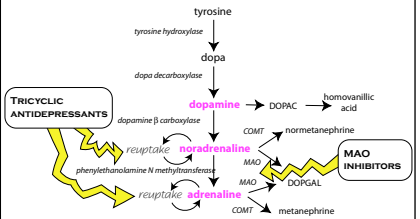
sites of drug action

- 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

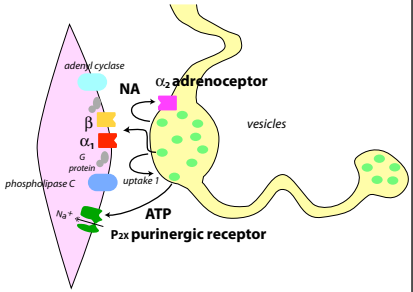
- synthesis
- storage
  - reserpine
    - blocks uptake into vesicles
    - causes NA depletion
- release
- receptor binding
- uptake

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
α1	adrenaline	vasoconstriction noradrenaline	phenylephrine mydriasis	prazosin
α2	adrenaline	(vasodilatation) noradrenaline atipamezole	xylazine sedation & analgesia	yohimbine
	detomidine			
β1	adrenaline	+ve inotropy (noradrenaline)	dobutamine tachycardia	atenolol
	dopamine		metoprolol	
β2	adrenaline	bronchodilatation	salbutamol	propranolol
			vasodilatation (musc)	
	clenbuterol	(nonselective)		uterine
relaxation				
(β3	adrenaline	lipolysis	SR58611A	SR59230A)

α2 adrenoceptors

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

clinical use of agonists

- heart failure
  - adrenaline & β1 agonists
- anaphylactic reactions
  - adrenaline
- delay parturition
  - clenbuterol
- sedation and analgesia
  - xylazine and α2 agonists

clinical use of antagonists

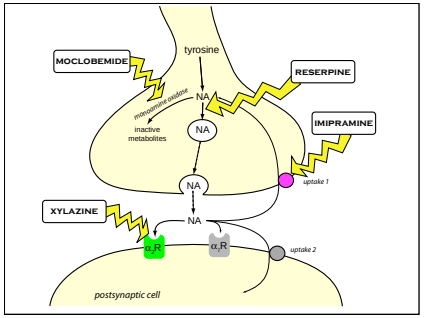
- slow heart
  - β1 blockers
- (vasodilatation)
  - α1 blockers
- reversal of α2 sedation
  - α2 blockers

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

- 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??

fast

ATP

noradrenaline

peptide co-transmitters

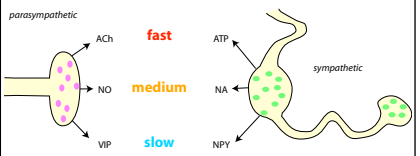
inflammatory mediators

slow

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**

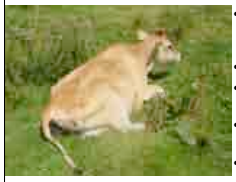
oxides of nitrogen

- nitric oxide - NO
  - vasodilator & neuromodulator
- nitrous oxide - N_2O
  - anaesthetic gas
- nitrogen dioxide - NO_2
  - environmental pollutant

NANC transmission

- nitric oxide
  - nitrergic neurones

downer cow



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

noradrenergic 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