

## ADRENERGIC TRANSMISSION

### Adrenergic Agonists

Nor adrenaline	$\alpha > \beta$	Endogenous agonist
Adrenaline	$\beta > \alpha$	Emergency treatment for anaphylactic shock, asthma, cardiac arrest
Isoprenaline	$\beta$ non selective	Was used for asthma but tachycardia side effect
Phenylephrine	$\alpha$ 1 selective	Nasal decongestant, but hypertension
Clonidine	$\alpha$ 2 selective	Hypertension – by reducing NA release
Dobutamine	$\beta$ 1 selective	Cardiogenic shock – increase cardiac contractility. But may cause dysrhythmias
Salbutamol	$\beta$ 2 selective	Asthma, premature labour, skeletal muscle tremor
$\alpha$ -methylnoradrenaline	$\alpha_2 \gg \alpha_1$	Enter vesicles exchange for NA, is a false transmitter. Less active on $\alpha_1$ than NA so less vasoconstriction and potent on $\alpha_2$ causing powerful presynaptic inhibitory feedback. Antihypertensive during pregnancy. Can cause drowsiness, diarrhoea... See methyl dopa

### Adrenergic Antagonists

Phenoxybenzamine + Phentolamine	$\alpha$ non selective	Peripheral vascular disease (promotes dilatation) and phaeochromocytoma – catecholamine secreting tumour. But hypotension and reflex bradycardia
Prazosin	$\alpha$ 1 selective	Hypertension (postural hypotension and impotence)
Yohimbine	$\alpha$ 2 selective	Not used clinically
Propranolol	$\beta$ non selective	Angina, hypertension, dysrhythmias, glaucoma (but bronchoconstriction, fatigue, depression, hypoglycaemia)
Atenolol	$\beta$ 1 selective	Reduces effect of exercise and excitement on HR (lower effect on bronchoconstriction, similar side effects to propranolol)
Butoxamine	$\beta$ 2 selective	No clinical uses

### Drugs affecting NA biosynthesis and storage

$\alpha$ -methyl tyrosine	Inhibits tyrosine hydroxylase
Carbidopa	Inhibits dopa decarboxylase
Methyl dopa	Taken up by neurones and metabolised by dopa

	decarboxylase and DBH to $\alpha$ -methylnoradrenaline (see agonists)
Disulfiram	Inhibits dopamine beta hydroxylase causing partial depletion of NA stores
Reserpine	Depletes NA stores by inhibiting vesicular uptake of NA (formerly used as antihypertensive but central effects cause depression)

#### Drugs that affect uptake and metabolism

Tricyclic antidepressants, e.g. Imipramine	Inhibits uptake 1	Enhancement of sympathetic effects, used for depression
Cocaine	Inhibits uptake 1 (neuronal); local anaesthetic	Analgesia; CNS stimulation. But can cause hypertension, convulsions and dependence
Phenoxybenzamine / corticosteroids	Inhibit uptake 2 (non neuronal)	
Clorgyline	MAO-A inhibitor	Increase cytoplasmic concentration of catecholamines in nerve terminal. Can be used for depression. Potentiates sympathetic effects
Selegiline	MAO-B inhibitor	Same as above. Used to treat Parkinsons – by potentiating remaining dopamine in SN neurones
Phenelzine, iproniazid, tranylcypromine	Non selective MAO inhibitor	As above. Irreversible, associated with the cheese effect.
Entacapone	COMT inhibitor	Similar to MAO B – used for parkinsons
Guanethidine	Inhibits NA release, causes NA depletion.	Enters by uptake 1 – competing with NA, accumulated by synaptic vesicles displacing NA this initial action potentiates the sympathetic response (e.g. initial hypertension). When given at low dose chronically depletes NA stores, and is itself released at terminal – neurone blocking action. Large dose directly inhibits exocytosis by preventing fusion. Used for hypertension in past.

#### Indirectly acting sympathomimetic amines

Tyramine	Enter terminal via uptake 1 and then compete with NA for uptake into vesicles, displacing NA	NA release. Present in many foods – e.g. cheese
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Amphetamine	As above. Also inhibits uptake 1, and also inhibits MAO to potentiate effect	NA release, CNS stimulant. Drug of abuse, can cause insomnia, hypertension, tachycardia (MDMA same effect but selective for 5-HT)
Ephedrine	As tyramine. Also acts as $\beta$ 2 agonist	$\beta$ 2 effect - used as nasal decongestant. Otherwise similar to above

NOTE indirectly acting sympathomimetic amines are contraindicative with MAO inhibitors. Strongly potentiated sympathetic response causing massive hypertension. "Cheese effect" (eating cheese (tyramine) whilst taking MAO inhibitors)