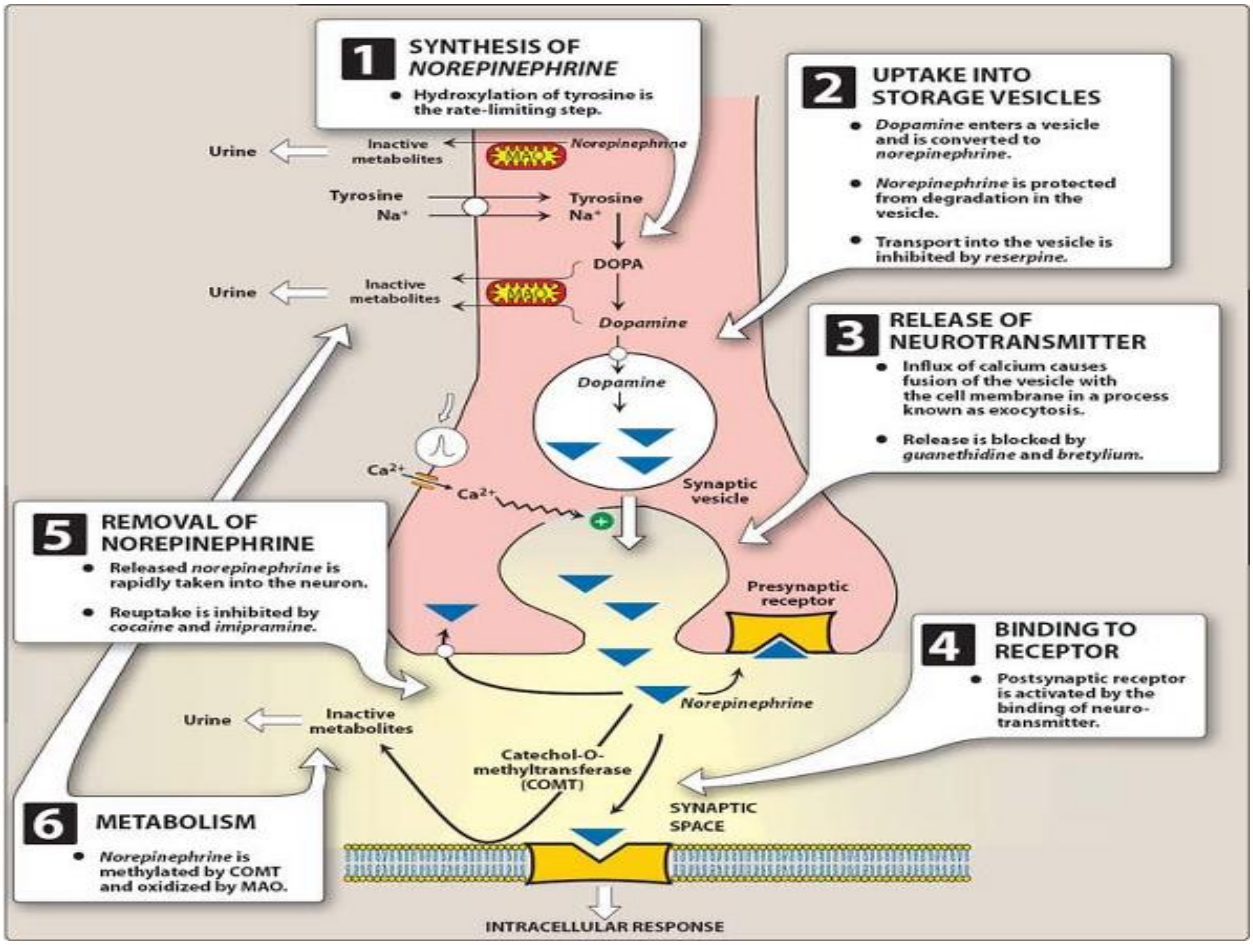
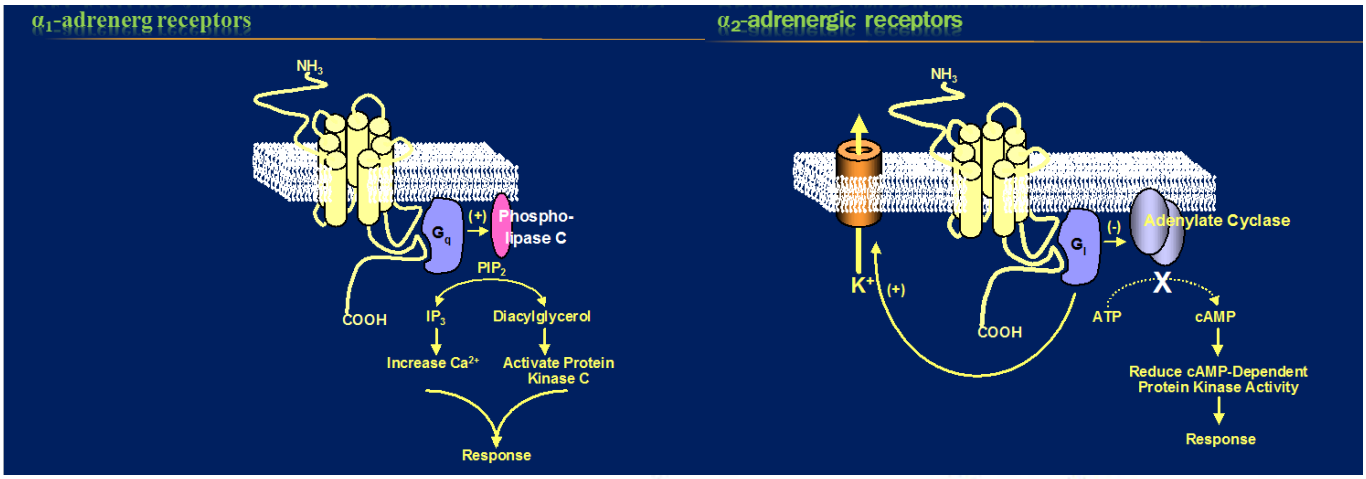
Adrenergic System

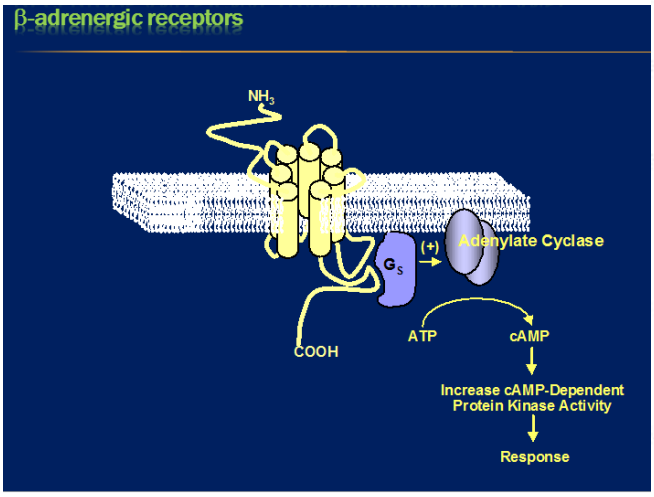


Adrenergic Receptors

The two types of adrenergic receptors are alpha and beta

- Each type has two or three subclasses
  ($\alpha1$, $\alpha2$, $\beta1$, $\beta2$, $\beta3$)
- Effects of NE binding to:
  - α receptors is generally stimulatory
  - β receptors is generally inhibitory
- A notable exception – NE binding to β receptors of the heart is stimulatory (Remember β blockers?)





Adrenoceptors

Sub-type	Location of receptors	Type of G-protein coupled to receptor	Basic pathway
α1	Smooth Muscle	Gq	Increase in PLC Increase in IP3 Increase in intracellular Ca2+ => m. contraction
α2	Presynaptic nerves	Gi	Decrease in activation of Adenylate cyclase Decrease in cAMP
β1	Heart	Gs	Increase in activation of Adenylate cyclase, Increase in cAMP Increase in intracellular signaling pathways
β2	Smooth muscle		
β3	Fat tissue		

Adrenergic receptors

Receptor	Location	Effect
α_1	Postsynaptic in smooth Muscle of Blood vessels GIT & Urinary Sphincters	 Vasoconstriction contraction
α_2	Presynaptic	↓ NA release, ▼ insulin
β_1	Heart Kidney	↑ Rate and Contraction ↑ Renin release
β_2	Smooth Muscle of Blood vessels Bronchi Intestine Urinary & Uterus Liver, muscles	 Relaxation Relaxation Relaxation Relaxation glycogenolysis
β_3	Adipose tissue	Lipolysis

adrenergic agonists

Drug	Action (receptors)	Selected therapeutic uses and important remarks
Catecholamine*		
Adrenaline	$\alpha_1, \alpha_2, \beta_1, \beta_2$	Acute asthma, open angle glaucoma, anaphylactic shock, in local anaesthetics to increase duration of action
Noradrenaline	$\alpha_1, \alpha_2, \beta_1$	Shock
Isoprenaline	β_1, β_2	Asthma, severe bradycardia, heart block, sinus bradycardia
Dopamine	dopaminergic β_1	Shock, decreased renal function Congestive heart failure
Dobutamine	β_1	Congestive heart failure
Non-catecholamines▲		
Phenylephrine	α_1	Nasal congestion, hypotension
Methoxamine	α_1	Hypotension (during surgery, does not produce cardiac arrhythmias in sensitised heart, i.e. no beta activity) Paroxysmal supraventricular tachycardia
Clonidine	α_2 (CNS)	Hypertension, withdrawal from opiates or benzodiazepines
Salbutamol Terbutaline Ritodrine	β_2	Asthma (bronchospasm), premature labour (they have short onset and duration of action)
Salmeterol Formoterol	β_2	Asthma (they have slow onset and long duration of action)
Amphetamine	α, β (CNS)	Attention deficit (hyperkinetic) disorder (in children)
Ephedrine	$\alpha_1, \alpha_2, \beta_1, \beta_2$ (CNS)	Nasal congestion, asthma

adrenergic antagonists (sympatholytic agents)

Drug	Action (receptors)	Selected therapeutic uses and important remarks
α-adrenoceptor antagonists		
Phenoxybenzamine	α_1, α_2 (blocking)	Pheochromocytoma, Raynaud's disease (irreversible block)
Phentolamine	α_1, α_2	Diagnosis of pheochromocytoma (competitive block); it induces reflex tachycardia. (by vasodilatation and blocking autoregulatory α_2 receptors)
Prazosin		Hypertension [first dose effect, syncope (fainting)]
Terazosin Doxazosin[1]	α_1	Benign prostatic hyperplasia
Tamsulosin	α_{1c}	Benign prostatic hyperplasia (Not for hypertension) Ureteral colic
β-adrenoceptor antagonists[2]		
Propranolol	β_1, β_2	Hypertension, migraine, hyperthyroidism, pheochromocytoma, angina pectoris, myocardial infarction
Timolol	β_1, β_2	Glaucoma, hypertension
Acebutolol Atenolol Metoprolol	β_1	Hypertension
Pindolol	β_1, β_2	Hypertension
Labetalol	β_1, β_2, α_1	Pheochromocytoma (hypertension)
Carvedolol	β_1, β_2, α_1	Angina pectoris, cardiomyopathy, (heart failure, hypertension) Higher ratio of β to α blockade than labetolol

Drugs affecting neurotransmission

Drugs affecting neurotransmitter release or re-uptake		
Reserpine	Disrupts storage of amines causing depletion of amines	Hypertension (no longer used because of adverse-effects like depression)
Guanethidine	Adrenergic neurone blocking agent	Hypertension (no longer used because of adverse-effects, orthostatic hypotension, male sexual dysfunction
Cocaine	Neuronal amine re-uptake (U_1) blocker	CNS stimulant (drug abuse)