**Adrenergic mechanisms**
The sympathetic nervous system is an important regulator of the activities of organs. The effects of sympathetic stimulation are mediated by release of catecholamine (Adrenaline, noradrenalin and dopamine) from nerve terminals that to activate the adrenoceptors on postsynaptic sites. Also in response to a variety of stimuli such as stress, the adrenal medulla releases Adrenaline, noradrenalin which is transported in the blood to target tissues.

**ADRENOCEPTORS**

**Beta (β) Adrenoceptors**
Subtypes of β receptors, designated (β₁), (β₂) and (β₃) receptors

**Alpha Adrenoceptors**
two major groups of α receptors α₁ and α₂ (Auto receptor)

**Dopamine Receptors**
The dopamine receptor subtypes, termed D₁, D₂, D₃, D₄, and D₅

**Selectivity for Adrenoceptors**
The classification of sympathomimetics and antagonists is based on selectivity for receptors and on use. But selectivity is relative, not absolute; some agonists act on both α- and β receptors.

**Sympathomimetic drugs**
Drugs that mimic the actions of (Adrenaline, noradrenalin and dopamine) have a wide range of effects, which can be grouped by mode of action and receptors that they activate.

**Directly**
By binding on adrenoceptors: as agonists (adrenaline) or antagonists (propranolol)
Indirectly Sympathomimetic drugs

1- Discharging noradrenalin stored in nerve endings (amphetamine)
2- By preventing reuptake into the adrenergic nerve ending of released noradrenaline and dopamine (cocaine, tricyclic antidepressants and noradrenaline-selective reuptake inhibitors)
3- By preventing the destruction of catecholamine in the nerve ending (mono amine oxidase) inhibitors
4- By depleting the stores of noradrenalin in nerve endings (reserpine)
5- By preventing the release of noradrenalin from nerve endings in response to a nerve impulse (guanethidine)
6- By activation of adrenoceptors on adrenergic nerve endings that inhibit release of noradrenaline (α2 autoreceptors) (clonidine)
7- By blocking sympathetic autonomic ganglia (trimetaphan).

EFFECTS OF SYMPATHOMIMETIC DRUGS

Cardiovascular System

A. BLOOD VESSELS: Alpha receptors increase arterial resistance, whereas β2 receptors promote smooth muscle relaxation

B. HEART: Stimulation of β receptors increases rate and cardiac output

C. BLOOD PRESSURE: The effects on blood pressure can be explained on the basis of their effects on the heart, blood vessels

Eye: The radial pupillary dilator muscle of the iris contains α,β receptors; activation causes mydriasis
Respiratory Tract: Bronchial smooth muscle contains $\beta_2$ receptors that cause relaxation. Activation of these receptors results in bronchodilation.

Gastrointestinal Tract: Relaxation of GIT smooth muscle by $\alpha$, $\beta$ stimulant agents.

Genitourinary Tract: uterus contains $\beta_2$ receptors. mediate relaxation may be clinically useful in pregnancy. The bladder base, urethral sphincter, and prostate contain $\alpha$ receptors that mediate contraction and promote urinary continence. The $\beta_2$ receptors of the bladder wall mediate relaxation.

Metabolic Effects: Activation of $\beta_3$ adrenoceptors in fat cells leads to increased lipolysis.

Effects on Endocrine Function: insulin secretion is stimulated by $\beta$ receptors and inhibited by $\alpha_2$ receptors.

Individual sympathomimetics

CATECHOLAMINES

Adrenaline (epinephrine)

Adrenaline ($\alpha$ - and $\beta$-adrenoceptor effects)

very potent vasoconstrictor and cardiac stimulants

Noradrenaline (norepinephrine)

(chiefly $\alpha$ and $\beta$ effects). The main effect of administered noradrenaline is to raise the blood pressure by constricting the arterioles and so raising the total peripheral resistance.
**Dopamine and Dobutamine**

It is useful in shock and in low output heart failure

**NONCATECHOLAMINES**

Salbutamol (Ventolin)

is taken orally, 2-4 mg up to 4 times/day; it also acts quickly by inhalation and the effect can last as long as 4h, which makes it suitable for both prevention and treatment of asthma.

premature labour. (Salmeterol have low onset and long duration of action)

**Ephedrine**

Ephedrine is indirect sympathomimetic actions Ephedrine can be used as a bronchodilator, in heart block, as a mydriatic and as a mucosal vasoconstrictor, but newer drugs, which are often better for these purposes, are displacing it

**Mucosal decongestants**

Nasal and bronchial decongestants (vasoconstrictors) are used in allergic rhinitis, colds, coughs and sinusitis, as nasal drops or nasal sprays. All the sympathomimetic vasoconstrictors, have been used for the purpose, Ischaemic damage to the mucosa is possible if they are used excessively (more often than 3-hourly) or for prolonged periods (> 3 weeks)

**Shock**

Definition. Shock is a state of inadequate capillary perfusion (oxygen deficiency) of vital tissues to an extent that adversely affects Vital organs function, brain (consciousness, respiration) and kidney (urine formation): heart(pump blood)
Adrenoceptor Antagonist Drugs

PHARMACOLOGY OF THE $\alpha$-RECEPTOR ANTAGONIST DRUGS

Alpha-receptor antagonists may be reversible or irreversible in their interaction with these receptors. Phentolamine, prazosin are examples of reversible antagonists. Phenoxybenzamine, an irreversible blockade


Pharmacologic Effects

A. CARDIOVASCULAR EFFECTS

$\alpha$-receptor antagonist drugs cause a lowering of peripheral vascular resistance and lowering blood pressure.

B. OTHER EFFECTS

Minor effects that the blockade of $\alpha$ receptors in other tissues include miosis and nasal stuffiness.

CLINICAL USES

Pheochromocytoma.
Hypertensive Emergencies'
Chronic Hypertension
Peripheral Vascular Disease
Local Vasoconstrictor Excess
Urinary Obstruction
Erectile Dysfunction
**BETA-RECEPTOR ANTAGONIST DRUGS**

Beta-receptor antagonists antagonizing the effects of catecholamine's at β adrenoceptors. occupy β receptors and competitively reduce receptor occupancy by catecholamine's and other β agonists.

The major difference among the many β-receptor-blocking drugs concerns their relative affinities for β₁ and β₂ receptors. Some of these antagonists have a higher affinity for β₁ than for β₂ receptors, and this selectivity may have important clinical implications. Since none of the clinically available β-receptor antagonists are absolutely specific for β₁ receptors, the selectivity is dose-related; it tends to diminish at higher drug concentrations.

**Pharmacodynamics of the Beta-Receptor-Antagonist Drugs**

**A. EFFECTS ON THE CARDIOVASCULAR SYSTEM**

Beta-blocking drugs lower blood pressure in patients with hypertension.

**B. EFFECTS ON THE RESPIRATORY TRACT**

Blockade of the β₂ receptors in bronchial smooth muscle may lead to an increase in airway resistance, particularly in patients with asthma. Beta₁-receptor antagonists such as metoprolol and atenolol may have some advantage over nonselective β antagonists. However, no currently available β₁-selective antagonist is sufficiently specific to completely avoid interactions with β₂ adrenoceptors.

**C. EFFECTS ON THE EYE**

Several β blocking agents reduce IOP especially in glaucoma.

**D. METABOLIC AND ENDOCRINE EFFECTS**

Beta-receptor antagonists such as propranolol inhibit lipolysis.

**E. EFFECTS NOT RELATED TO BETA-BLOCKADE**

Local anesthetic action, also known as "membrane-stabilizing" action, is a prominent effect of several β blockers.
SPECIFIC AGENTS

Propranolol
Metoprolol, Atenolol,
Timolol
Betaxolol
Carvedilol
Esmolol
Butoxamine

CLINICAL USES OF THE β RECEPTOR-BLOCKING DRUGS

Hypertension
Schematic Heart Disease
Cardiac Arrhythmias
Glaucoma
Hyperthyroidism
Neurologic Diseases

Adverse effects of β RECEPTOR-BLOCKING DRUGS

The major adverse effects of β-receptor antagonist drugs relate to the consequences of β blockade. Beta₂-receptor blockade associated with the use of nonselective agents commonly causes worsening of asthma and other forms of airway obstruction without having these consequences in normal individuals. If at all, in patients with reactive airways. Beta₁-selective antagonists are generally well tolerated.