* Cholinergic agonists
* Classify & describe cholinergic agonists including actions, therapeutic uses & adverse reactions.
* Describe myaesthenia gravis & its management
* Explain Organophosphorous poisoning & treatment
* Cholinergic agonist- Classification

**Direct Acting Cholinergic Drug**

* Acetylcholine
* Bethanechol.
* Pilocarpine.
* Methacholine

**Indirect Acting Cholinergic Drugs (Cholinesterase ors)**

* **Reversible: *water soluble-***  Neostigmine, Edrophonium

 Pyridostigmine,

  ***Lipid soluble-*** Physostigmine, Donepezil, Tacrine, Gallantamine

* **Irreversible.-**  Organophosphorous Compounds, Echothiophate, malathion, parathion, tabun

**Reactivation of acetylcholinesterase-** Pralidoxime

* ***Actions of acetylcholine***

**Muscurinic actions:**

***Heart:*** it decreases the heart rate and cardiac output.

***Blood vessels:*** it causes vasodilatation and decreases BP.

***GIT*:** It increases the salivary & intestinal secretion.

 Increases intestinal motility and relaxes sphincters

***Respiratory system*:**  bronchoconstriction & Increased secretions.

***Eye*s**: it causes:

* Miosis.
* Accommodation of near vision.
* Decrease the IOP due to increase in the out flow of aqueous humor.

***Genitourinary tract*:** it causes:

* Urination.
* Erection of genital in male.
* *CNS*: it causes excitatory effect and effect on the learning, short term memory and arousal.
* **The nicotinic actions:**

**NMJ:** contraction of skeletal muscles.

* Stimulates both sympathetic and parasympathetic ganglia.
* Stimulates the release of adrenaline from the adrenal medulla and chromoffin.
* **In CNS**: stimulates the release of ADH at the hypothalamus.

***Therapeutic uses:***

* Uses as eye drop to produce rapid and complete miosis after cataract surgery**.**
* **BETHANECHOL**
* Not hydrolyzed by acetylcholinesterase but it is hydrolyzed by other esterase.
* It has no nicotinic actions.
* It is longer duration of action than acetylcholine.
* ***Therapeutic uses:***
* Post operative non-abstractive urinary retention.
* Post-operative ileus.
* **PILOCARPINE**

It is natural alkaloid, not hydrolyzed by acetylcholinesterase.

It has marked muscarinic actions.

***Actions:***

* **Eye:** loss of accommodation, miosis and lowering the intraocular pressure (IOP).
* **Other actions:** it stimulates the secretary glands and causes sweating, salivation and lacrimation.

***Therapeutic uses of pilocarpine:***

* In the treatment of GLAUCOMA.
* To reverse cycloplagic and mydriatic effect of atropine.

***Side effects:***

* CNS disturbance because it is crossing the BBB.
* Sweating and salivation.
* **PHYSOSTIGMINE:**
* **It is an alkaloid.**
* **Well absorbed and penetrate the BBB.**

***Therapeutic uses:***

* **Glaucoma.**
* **Atropine poisoning**
* **Alzheimer s disease.**

***Side effects:***

* **CNS: convulsions.**
* **Heart: bradycardia.**
* **Paralysis of skeletal muscles which it is rare seen in the therapeutic dose.**
* **Lid muscles twitching.**
* **It is synthetic anticholinergic drug.**
* **It is poorly absorbed.**
* **It is polar compound and so that not cross to the CNS.**

***Therapeutic uses****:*

* As antidote for tubocurarine poisoning
* Management of Mysthenia Gravis:

it is an a autoimmune disorder due to antibodies against Ach receptor,

* **. Organophosphorous compounds**
* They are irreversible anticholinesterase:
* They are insecticides and nerve gases.
* They include: parathion, malthion, and sarin.
* They are highly lipid soluble compounds. So that they cross the BBB.
* Management of myaesthenia gravis
* Management of myaesthenia gravis(contd.)
* ***Toxicity / poisoning of organophosphorous compounds:***
* ***Mechanism of toxicity:***
* **They inactivate enzyme ACHE irreversibly and increase the level of acetylcholine.**

***Actions:***

* **Acute toxicity: paralysis of respiratory muscle and excessive bronchial secretion.**
* **Chronic toxicity: neuropathy and demyelination of axons.**
* ***Treatment of organophosphate poisoning***
* **Maintenance of vital signs:** aspiration of bronchial secretions, endotracheal intubations and artificial respiration.
* **Decontamination:** to prevent further absorption, removal of the contaminated clothes and washing the skin, gastric lavage if need.
* **atropine:**
* **Cholinesterase reactivator Examples:** pralidoxime (PAM).
* Diazepam.
* **References**
* Lippincott’s Illustrated review of pharmacology – 4th edition
* Basic & clinical pharmacology, Bertram G katzung-12th edition
* Goodman & Gilman’s –pharmacology
* Internet resource