Unit II

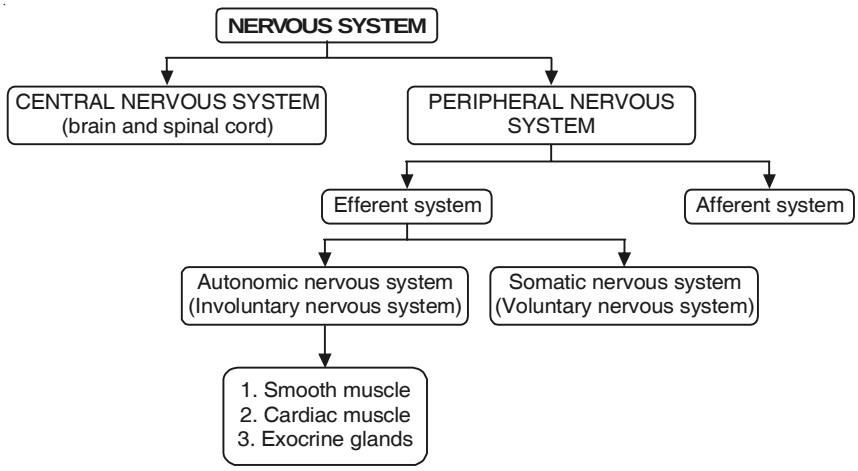
Drugs Affecting on Autonomic Nervous System

- Neurotransmitters have an ability to initiate the impulse propagation. Certain substances do not initiate the process of the impulse transmission but can be modify it. Such substances are termed as modulators of transmission. For example, most of the autonomic drugs act either by mimicking or modifying the action of the neurotransmitter released by the autonomic fibers at either synaptic cleft or effector cells, besides this, the nerve cell is provided with a number of feedback control systems which regulate the biosynthesis, release and metabolism of the neurotransmitter and thus exercise a control over the biological response.

AUTONOMIC NERVOUS SYSTEM (Flow Chart 10.1)

- The ANS consists of central and the peripheral components. It is evident from the investigation that elicitation of autonomic reflexes (e.g. blood pressure changes, vasomotor response to alteration of body temperature, sweating, constriction of urinary bladder) can occur at the level of the spinal cord.
- However, integration of much autonomic function occurs at supraspinal levels. Thus, regulation of respiration and blood pressure is integrated in medulla. The hypothalamus plays a prominent role in medulla. The hypothalamus plays a prominent role in integration of various autonomic functions, e.g. regulation of blood pressure, sleep, emotions, sexual reflexes carbohydrate and fat metabolism.
- Posterior and lateral hypothalamic nuclei are connected with the sympatho-adrenal system, while anterior and midline nuclei are concerned with parasympathetic functions. The posterior-medial hypothalamus is involved in the modulation of the baroreceptor reflex.
- The other higher centeres involved in the integration of various autonomic functions include the neo-startum, limbic system and cerebral cortex.
- The autonomic nervous system (ANS) controls all involuntary actions aimed to maintain the constancy of the internal environment. It provides a homeostasis for the regulation of all metabolic changes which are essential for life. The ANS is termed as the visceral, vegetative or involuntary nervous system. In the periphery, it functions through, ganglia, plexus and regulates autonomic functions which are not under the conscious control.

Flow chart 10.1: Classification of nervous system



- These include breathing, regulation of the cardiovascular system, glandular secretion, digestion, body temperature and metabolism. Except skeletal muscles, all innervated organs

NERVES OF PERIPHERAL SYSTEM

- The nerves in the peripheral nervous system (Fig. 10.5) are classified on the basis of their function into:
  1. Sensory (afferent) neuron.
  2. Motor (efferent) neuron.
  3. Internuncial neuron.
- Sensory neurons transmit impulse from CNS to or towards the muscle or tissues.
- Internuncila neurons are located in CNS and they transmit impulse from sensory to the motor neurons.
- Many neurotransmitter play an important role in the propogation of the nerve impulse in the sensory neurons. These include substance P, Somatostatin, Vasoactive intestinal polypeptides and Cholecytokinin.

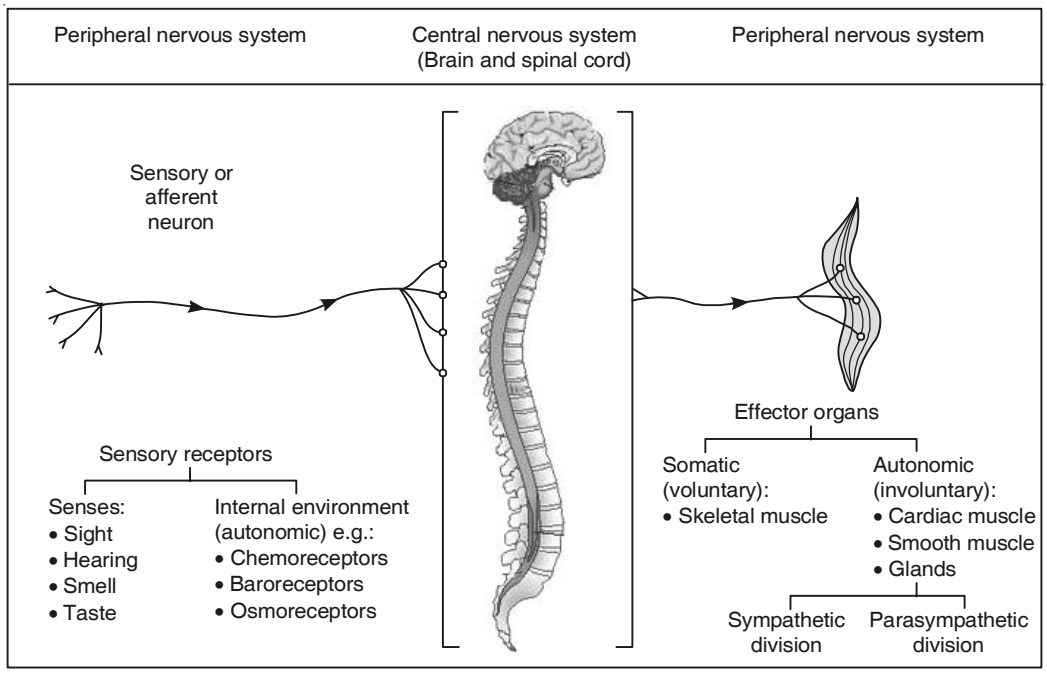


Fig. 10.5: Peripheral nervous system

Efferent Nervous System of ANS (Fig. 10.6)

- The efferent (motor) nervous system of ANS can be broadly categorized into;
  1. Parasympathetic (or craniosacral) division.
  2. Sympathetic (or thoracolumbar) division.
- This classification is mainly based upon the type of neurotransmitters that predominant in each division.
- The cholinergic nervous system consists of preganglionic and post-ganglionic fibers. The preganglionic fibers have their origin in midbrain, medulla oblongata and the sacral part of the spinal cord. Thus, the principal site of control and co-ordination of both sympathetic and para-sympathetic nervous systems is hypothalamus.

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Parasympathomimetics (Cholinergic Agents)

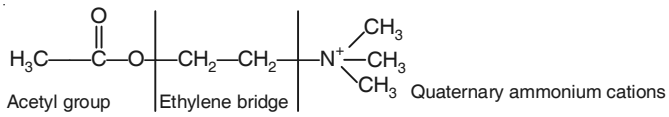
Cholinergic agents are drugs that either directly or indirectly produce effect similar to those elicited by acetylcholine (ACh).

- Acetylcholine was first synthesized by Bayer in 1867. In general, stimulation of parasympathetic nervous system induces constriction of pupil and bronchi, decrease in heart activity and an increase in the activity of digestive system, i.e. salivation, GIT secretion are promoted and motility of the intestine is also increased.

CHEMICAL FEATURE OF ACETYLCHOLINE

Following are some of the important chemical feature of acetylcholine molecule.

1. Chemically, it is an ester of acetic acid and choline, an amino alcohol.
2. On the structural basis, it offers three sites for molecular modification.
   a. Acetyl group.
   b. Ethylene bridge.
   c. Quaternary ammonium group.



3. The quaternary nitrogen atom bearing a strong positive charge in the center of the so called cationic head and gives acetylcholine (ACh) its basic character. The cationic head fits into a depression in the receptor surface, the anionic site, which bears a negative electrical charge.
4. The alkylamine chain provides a bridge of the correct length between the cationic head and acetyl group of the ACh molecule. Increase or decrease in the length of the alkylamine chain markedly reduces the muscarinic potency.
5. The acetyl group forms the third part of the ACh molecule and bears an overall negative charge. This group is thought to fit into a depression in the receptor surface bearing a positive charge and called esteratic site.
6. Acetylcholine is stable in acidic solution but it is very unstable in alkaline media.
7. Free acetylcholine presents in the tissue fluid and in circulation it is rapidly hydrolysed to acetic acid and choline molecules by cholinesterase enzyme.
8. Acetylcholine exhibits some of its actions via muscarinic receptors while remaining action is propagated through nicotinic receptors.