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Lecture 1

NERVOUS SYSTEM

The Nervous System is the most complex system in the body histologically and physiologically. It is formed by interconnected network of billions of ***neurons*** or nerve cells and supporting ***glial*** cells. In addition to the cells, there are many blood vessels that are separated from the nervous tissue by the ***blood brain barrier.***

Nerve tissue is distributed throughout the body as an integrated communications network, this system then, ***creates, analyzes, identifies and integrates the information***.

The Nervous System is capable of:

1. Responding to the ***external environment***, ranging from the simple reflex arc in the spinal cord, to the complex operations of the brain e.g. memory of past experience
2. Through the ***autonomic nervous*** system, it regulates:
3. The functions of the hollow viscera e.g. smooth muscle contraction in the blood vessels, gut, gall bladder, and urinary bladder.
4. The cardiac muscle contraction
5. Secretion of the glands

The regulation of the functions of the internal organs is through the cooperation between the nervous and endocrine system which is referred to as ***Neuroendocrine*** Tissue.

The functions of the nervous system depend on a fundamental property of neurons; ***Excitability or Irritability***. The resting neuron, as well as all other cells, maintains an ionic gradient across its plasma membrane, creating an ***electrical potential***. Excitability involves a rapid change in the plasma membrane permeability in response to appropriate stimuli. Neurons react promptly to stimuli such that the ionic gradient is reversed and the plasma membrane becomes ***depolarized***. The membrane depolarization propagates along the plasma membrane of the neuron. This propagation is called the ***action potential***, the depolarization wave, or the ***nerve impulse.*** This wave is capable of travelling long distances along the neuronal process to the effector organ.

The nervous system is divided anatomically into:

***Central Nervous System CNS***, consisting of:

\* The brain (cerebrum and cerebellum)

\*The spinal cord

***Peripheral Nervous System PNS***, consisting of:

Cranial

\*Nerves Spinal

Peripheral

\*Ganglia

Motor

\*Nerve endings

Sensory

*Ganglia are small groups of nerve cells outside the CNS*

The nervous system is divided functionally into:

* ***Somatic nervous*** ***system*** (all voluntary functions),
* ***Autonomic nervous system*** (involuntary functions).

***NEURON***

The Neuron or nerve cell is the functional unit in both the central and peripheral nervous system, there are more than 10 billion neurons in the human nervous system. Their structure consists of three parts:

\****The cell body, or perikaryon***, which is the synthetic or trophic center for the entire nerve cell and is the receptive to stimuli.

\****Dendrites,*** elongated processes specialized to receive stimuli from the environment, sensory epithelial cells, or other neurons

\****Axon*** (Gr. Axon, axis), is a single process specialized in generating and conducting nerve impulses to other cells (nerve, muscle, and gland cells). Axons may also receive information from other neurons. The distal portion of the axon is usually branched as the terminal arborization. Each branch terminates on the next cell in dilatations called ***end bulbs (boutons),*** which interact with other neurons or non nerve cells at structures called ***synapses***. Synapses initiate impulses in the next cell of the circuit.

Neurons and their processes vary in size and shape. The size can be very small, 4-5 microns in diameter (cells of the granular layer of the cerebellum), or very large up to 150 microns in diameter. They are three main groups;

* ***Sensory*** (afferent), convey impulses from receptors (external environment or from within the body) to the CNS,
* ***Motor*** (efferent), convey impulses from the CNS or the ganglia to the effector cells e.g. muscle fibers, exocrine or endocrine glands.
* ***Interneuron or internuncial*** neurons, forming a communicating network between sensory and motor neurons. 99.9% of the neurons fall in the group.

Neurons are classified according to the number of processes extending from the cell body

* ***Multipolar*** neurons have one axon and two or more dendrites, e.g. motor neurons and interneurons.
* ***Bipolar*** neurons have one axon and one dendrite, e.g. retina and ganglia of the vestibulocochlear nerve.
* ***Unipolar*** (pseudonipolar) neurons have one process, the axon that divides close to the cell body into two long processes. Sensory neurons in the dorsal root ganglia are unipolar.

The neurons do not divide; they must last for a lifetime!

***Cell Body (Perikaryon),***

is the part of neuron that contains the nucleus and surrounding cytoplasm. It receives a great number of nerve endings of other nerve cells. The nucleus is large, spherical or ovoid, euchromatic (pale - staining), with prominent nucleolus. The chromatin is finely dispersed reflecting the intense synthetic activity of the neuron. Binucleate cells are seen in the sympathetic and sensory ganglia.

***Nissl bodies*** (Chromatophilic substance), a characteristic feature present in the motor neuron, represent aggregations of rough endoplasmic reticulum rER and polyribosomes for the protein synthesis. ***Golgi apparatus*** is found adjacent to the nucleus and present only in the cell body. ***Mitochondria*** are numerous; found throughout the cell and axon terminal. Intermediate filaments ***neurofilaments*** and ***microtubules*** present in both perikaryon and processes, arranged in parallel bundles. The function of the neurofilament is to support the cell, while the microtubules for the axonal transport. ***Lipofuscin*** pigment consists of residual bodies due to lysosomal digestion.

***Dendrites***

Dendrites, (Gr.dendron, tree), are short and divide like branches of a tree. They are covered with many synapses and are principal signal reception and processing site on neurons. The arborization increases the receptive area of the neuron, and the branches become much thinner with further division. The dendrites of Pukinjie cells of the cerebellum receive 200.000 axon terminals.

The dendrites contain the same cytoplasmic contents of the perikaryon, but devoid of Golgi apparatus.

***Dendritic spines***, are short blunt structures 1-3 microns long projecting from dendrites, they are the receptor site of the synapse. They are related to adaptation, learning, and memory.

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***Axon***

Axons are long, single, cylindrical processes that originate from a conical-shaped region of the perikaryon; the ***axon hillock***, which is devoid of Nissl bodies and Golgi cisternae, and it is the site where all other organelles pass to the axon

The axon varies in length and diameter according to the type of neuron. It may have the length of up to 100cm e.g. motor neurons to the skeletal muscle ***(Golgi type I neurons).*** Interneurons of the CNS ***(Golgi type II neurons),*** have a short axon.

The plasma membrane of the axon is called ***axolemma*** and the contents are known as the ***axoplasm***.

The ***initial segment***, lies just between the apex of the axon hillock and the beginning of the myelin sheath. It is the site where excitatory and inhibitory stimuli are algebraically summed, resulting in the decision to propagate – or not to propagate – a nerve impulse i.e. generation of the ***action potential***. Axons have a constant diameter and do not branch profusely.

***Collateral branches***: are branches of the axon that connect with other group of cells. An axon may give rise to ***recurrent branches*** near the cell body i.e. that turns back to cell body and to other collateral branches

Axoplasm contains mitochondria, microtubules, neurofilaments, and some cisternae of sER (smooth Endoplasmic Reticulum). Rough Endoplasmic Reticulum rER and polysomes are absent.

There is a bidirectional transport of small and large molecules along the axon:

* ***Anterograde transport***, which carries materials from the perikaryon to the periphery, e.g. neurotransmitters, tubulin molecules, mitochondria…etc.
* ***Retrograde transport***, which carries materials from the axon terminals to the perikaryon, e.g. viruses and toxins.

The transport system may be distinguished as:

* ***A slow transport system***, which occurs at a rate of 0.2-4 mm/day. It is only anterograde transport system
* ***A fast transport system***, which occurs at a rate of 20-400mm/day. It both an anterograde and a retrograde system.

***Kinesin*** allows the anterograde transport, and ***Dynein***, allows the retrograde transport.

***Synapse***

Synapses (Gr. Synapsis, union) are specialized junctions for the transmission of nerve impulses from neuron to another neuron or other effector cell (muscle and gland) in a unidirectional way.

Synapses between neurons are classified as;

* Axodendritic, occurring between axon and dendrite
* Axoaxonic, occurring between axon and another axon
* Axosomatic, occurring between axon and the cell body
* Dedrodendrirtic, occurring between dendrites and dendrites

Synapses may be classified as ***chemical*** or ***electrical***:

***Electrical synapses*** transmit ionic signals through gap junctions i.e. conducting neuronal signals directly, and are prominent in cardiac and smooth muscles.

***Chemical synapses***, by which an electrical signal (impulse) is converted from the presynaptic cell into a chemical signal in the postsynaptic cell.

Synapses are not easily resolvable in ordinary light microscopic Haematoxylin and Eosin stain. They are demonstrated as oval bodies on the surface of neurons using special (silver) stain. Those oval bodies ***bouton terminal*** (Fr. terminal button) or ***end bulb***

With electron microcopy EM, the synapse has the following structures:

* ***Presynaptic axon terminal*** (terminal bouton) from which the neurotransmitter is released.
* ***Postsynaptic cell membrane*** with receptors for the transmitter and ion channels to initiate a new impulse
* 20-30 nm wide intercellular space called ***synaptic cleft*** separating the presynaptic and postsynaptic membranes

The cell membrane on each side of the synaptic cleft is slightly thickened and the terminal bouton contains mitochondria, microtubules, neurofilaments, and membrane bound vesicles 40-65nm in diameter (neurosecretory vesicles). The most common neurotransmitters are Acetylcholine Ach, Norepinephrine NE, Gamma amino butyric acid GABA, dopamine, serotonin, etc…….

The releases of neurotransmitter by the presynaptic component can cause excitation or inhibition of the postsynaptic membrane.

***Motor end-plate***

The motor end-plate or the ***neuromuscular junction*** is the innervating site of the skeletal muscle by the motor nerve. A motor neuron may innervate many muscle fibers, the neuron and the muscle fiber which it supplies is called the ***motor unit***. Motor end-plate has the same basic structure of the synapse. The axon is covered only by a thin extension from the cytoplasm of Schwann cell. Within the axon terminal numerous mitochondria and synaptic vesicles containing acetylcholine. Synaptic cleft is situated between the axon terminal and the muscle fiber. The sarcolemma is thrown into deep ***junctional folds*** or ***secondary synaptic clefts*** to increase the surface area.

***Myelin Sheath***

Is a lipid-rich layer surrounding the myelinated axon. Axons in the peripheral nervous system PNS are sheathed by ***Schwann cells*** or ***neurolemmocytes***. The sheath may or may not form ***myelin*** around the axon, depending on their diameter. Axons of small diameter are usually ***unmyelinated*** nerve fibers. Thicker axons are generally ***myelinated*** nerve fibers. Myelination is due to the concentric wrapping of the enveloping cells, forming ***myelin sheath***. In the central nervous system CNS, the axons are sheathed by ***oligodendrocytes*** which myelinates several axons. Unlike Schwann cells which myelinates only one axon

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***Myelin Sheath***

Myelin sheath is a lipid–rich layer surrounding the “***myelinated****”* nerve fibers. It is composed of concentrically wrapped layers of plasma membrane of ***Schwann cells (neurolemmocytes),*** pushing the nucleus and cytoplasm to the periphery. The myelin sheath is segmented (each segment is 0.08-0.1mm) due to numerous Schwann cells arranged along the length of the axon. The area where two adjacent Schwann cells meet is devoid of myelin, the ***node of Ranvier***. The node of Ranvier is covered with plasma membranes of the two adjacent Schwann cells. The myelin sheath is not compactly arranged around the axon, i.e. some cytoplasm is left between the membrane lamellae in some regions forming small islands or clefts; the ***Schmidt-Lanterman clefts***. When the myelinated nerve is examined with light microscope, the myelin sheath is dissolved, showing a pale area surrounding the densely stained, centrally located axon. With electron microscopic stains, the myelin sheath appears as electron-dense lines.

***Unmyelinated Fibers***

The unmyelinated nerve fibers are more abundant in the CNS, where the axons run free, while in the peripheral nervous system, the axons are enveloped within simple folds of Schwann cells.

***Neuroglia***

Or ***glial cells***, are the supporting cells within the CNS, and are 10 times more abundant than the neurons. Glial cells are smaller than the neurons; they provide an ideal environment for the neuronal activities. Only the nuclei of glial cells are seen in routine histological preparations, they are identified by immunocytochemical or heavy metal staining methods.

In the CNS, there is very little or no connective tissue. Instead, there is ***neuropil***, which is a dense network of fibers from processes of both neurons and glial cells that fill the interneuronal spaces.

The glial cells that are situated in the CNS are

* Oligodendrocytes, the myelin –forming cells of the CNS
* Astrocytes, provide physical and metabolic support for the neurons of the CNS
* Ependymal cells, line the cavities within the CNS
* Microglial cells, are immune-related activity

***Oligodendrocytes***

Oligodendrocytes produce myelin sheath that provides the electrical insulation for neurons in the CNS. The oligodendrocyte sends cytoplasmic processes that wrap around the axons in essentially the same way as Schwann cell does in the PNS. One oligodendrocyte may myelinate up to 50 axons. They are predominant in the CNS white matter.

***Astrocytes***

Astrocytes are the largest of the neuroglial cells, and the most numerous. They have radiating processes, and they are unique to the CNS. Two kinds of astrocytes have been identified:

* Protoplasmic astrocytes, which are more prevalent in the gray matter, have short and branched processes
* Fibrous astrocytes, which are more common in the white matter, have few and long processes

Both types of astrocytes contain prominent bundles of intermediate filaments composed of ***glial fibrillary acidic protein (GFAP)***. Astrocytes have supportive and metabolic functions as well as the support during embryonic development. They control the ionic environment of neurons.

Astrocytes have processes that extend between blood vessels and neurons, the processes are expanded, forming ***perivascular feet*** that cover capillary endothelial cells and contribute to the ***blood-brain barrier.*** The other expanded processes form a layer, the ***glial limiting membrane*** which lines the pia mater. In damaged areas, astrocytes proliferate to form scar tissue, and they absorb excess of neurotransmitters.

***Epedymal cells***

Ependymal cells are low columnar or cuboidal cells that line the fluid filled cavities of the CNS (ventricles of the brain and central canal of the spinal cord). The apical ends of ependymal cells have cilia and microvilli, to facilitate the movement of the cerebrospinal fluid CSF. And the two adjacent ependymal cells are joined by junctional complexes separating the lumen of the canal from the intercellular space. The basal ends of ependymal cells are elongated sending branches to the adjacent neuropil.

***Microglia***

Microglia are phagocytic, and less abundant than other glial cells. They are distributed throughout gray and white matter; they secrete cytokins and invade microorganisms. Microglia originates from blood monocytes and belongs to the same family as macrophages and antigen presenting cells.

Microglia have dense elongated nuclei that can be recognized by routine H&E preparations. When activated, they retract their processes and assume the morphological characteristics of a macrophage.

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***Central Nervous System CNS***

The principal structures in of CNS are the ***cerebrum***, ***cerebellum***, and the ***spinal cord***. It is soft, gel-like organ due to the absence of connective tissue. In the freshly sectioned tissue, white regions (white matter), and gray regions (gray Matter) are recognized. This difference in colour is due to the distribution of the nerve cell bodies, glial cells and the nerve axons. The nerve cell bodies, dendrites, the initial unmyelinated nerve axon and the glial cells are mainly present in the gray matter .Gray matter is the region where synapses are present. The white matter is composed mainly of the myelinated nerve axons together with the myelin-producing oligodendrocytes, it does not contain neurons, and the nerves are grouped into bundles or ***tracts***. Gray matter is prevalent mainly at the cortex of the cerebrum and cerebellum and the white matter is present in the central region. Islands of gray matter, ***nuclei***, are found in the deep region of cerebrum and cerebellum. The nervous tissue is devoid of connective tissue and very small amount of extracellular substance.

The ***cerebral cortex*** is composed of six layers and the neurons are arranged vertically. The most abundant neurons are the efferent ***pyramidal neurons***, which have different sizes. The main function of the neurons is integration of sensory information and the initiation of voluntary motor responses.

The ***cerebellar cortex***, which coordinates muscular activity throughout the body, has three layers, an outer ***molecular layer***, a central layer of very large neurons called ***Purkinje cells***, and an inner ***granule*** ***layer***. The Purkinje cell bodies are conspicuous in H&E stains and their dendrites extend throughout the molecular layer as a branching basket of nerve fibers. The granule layer is formed by very small neurons (the smallest in the body), which are packed together densely, in contrast to the neuronal cell bodies in the molecular layer which are sparse.

In cross section of the spinal cord, white matter is peripheral and gray matter is internal and has a general butterfly shape. In the center is an opening, the central canal, which develops from the lumen of the embryonic neural tube and is lined by ependymal cells. The gray matter forms the ***anterior horns***, which contain the motor neurons whose axons make up the ventral roots of spinal nerves, and the ***posterior*** ***horns***, which receive sensory fibers from neurons in the spinal ganglia (dorsal root). Spinal cord neurons are large and multipolar, especially the motor neurons in the anterior horns.

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***Meninges***

The meninges are membranes of connective tissue that invest and protect the brain and the spinal cord. They are the dura mater, arachnoid mater, and the delicate pia mater, the ***dura mater***, the outermost layer, is composed of dense fibroelastic layer that is strongly adhered to the periosteum of the skull. Within the dura mater of the skull are spaces lined by endothelium, the ***venous sinuses***, these sinuses receive blood from the cerebral veins and carry it to the internal jugular veins. The dura mater that envelopes the spinal cord is separated from the periosteum of the vertebrae by the ***epidural space***, which contains loose connective tissue, veins, and adipose tissue. The internal surface of the dura mater, as well as its external surface in the spinal cord, is covered by simple squamous epithelium of mesnchymal origin. The dura is closely applied to the arachnoid, and the ***subdural space*** can develop between the two layers.

***Arachnoid***

The arachnoid (Gr. Arachnoeides, cobweb or spider web), is a fibrous connective tissue layer in contact with the dura, and connected by trabeculae to the underlying pia mater. The arachnoid and pia are linked together and they are considered as one layer, the ***pia-arachnoid*** or ***leptomeninges***. The connective tissue of the arachnoid is devoid of blood vessels, and the cavities between these trabeculae, which are lined by flattened cells, is filled with cerebrospinal fluid CSF. This space is completely separated from the subdural space.

The subarachnoid space forms a hydraulic cushion that protects the central nervous system from trauma, and it is communicated with the ventricles of the brain. The CSF circulates continuously from the ventricles into the subarachnoid space. Arteries and veins passing to and from CNS pass in the subarachnoid space are loosely attached to the pia mater.

***Pia mater***

The pia mater is loose connective tissue contains many blood vessels. Although it is located close to the nerve tissue, it is attached to the surface of the brain and continues into the sulci and around the blood vessels. The pia mater is not in direct contact with the nervous tissue, astrocytes send their processes towards brain surface where they contact the basement membrane of the pia, forming the ***glia limitans***.

Blood vessels penetrate the CNS through tunnels covered by pia mater the ***perivascular*** spaces. The pia mater disappears before the blood vessels break into capillaries (no pia mater around capillaries in CNS)

***Blood-brain barrier***

The blood-brain barrier is a functional barrier that prevents the passage of some substances, such as antibiotics and chemicals and bacterial toxic matter, from the blood to the nerve tissue.

The CNS capillaries are impermeable to certain plasma constituents, especially large molecules. This characteristic feature for the capillaries of the CNS is due to:

1. Occluding junctions between endothelial cells of the capillaries
2. The endothelial cells are not fenestrated with very few pinocytotic vesicles
3. Astrocyte foot processes

The capillaries of the choroid process, neurohypophysis, and the vomiting center of the hypothalamus are devoid of this barrier.

***Choroid Plexus***

Choroid plexus is a vascular structure consists of invaginated folds of pia mater, rich in dilated fenestrated capillaries that arise from the walls of the brain ventricles. It is covered with simple cuboidal to low columnar epithelium, with characteristics of ion transporting cells. Choroid plexus is found in the roofs of the third and fourth ventricles, and in the walls of the lateral ventricles. It is responsible for the production of cerebrospinal fluid CSF. CSF drains from these interconnected cavities via three channels between the fourth ventricle and the subarachnoid space which surrounds the CNS.

CSF is produced at a constant rate; it completely fills the ventricles, central canal of the spinal cord, subarachnoid space, and perivascular space. It is reabsorbed from the subarachnoid space into the superior sagittal venous sinus via finger-like projections called the arachnoid villi. (There are no lymphatic vessels in brain nerve tissue)

Cerebrospinal fluid is a clear, has low density (1.004-1.008g/ml), and is very low in protein content. A few desquamated cells and 2-5 lymphocytes per milliliter are present.

CSF is important for metabolism of the CNS and protects against mechanical shocks.

***Autonomic Nervous System***

The autonomic (Gr. Autos, self, +nomos, law) nervous system is related to the control of smooth muscle, secretion of some glands, and the modulation of the cardiac rhythm. Its function is to maintain constant internal environment (homeostasis). The term “autonomic” covers all neural elements concerned with visceral functions.

The autonomic nervous system is classified into three divisions

* Sympathetic division
* Parasympathetic division

Anatomically, the autonomic nervous system is composed of collection of nerve cell bodies located in the central nervous system. The main difference between the efferent flow of impulse to the skeletal muscle (the somatic effector) and the efferent flow to smooth muscle or cardiac muscle(the visceral effector), is that one neuron conveys the impulses from the CNS to the somatic effector, whereas a chain of two neurons carry impulses from the CNS to the visceral effectors. Therefore, there is presynaptic or (preganglionic) neuron and postsynaptic or (postganglionic) neuron.

***The sympathetic system***

The nuclei of the sympathetic system are located in the thoracic and lumbar segments of the spinal cord. The preganglionic fibers leave the CNS with the ventral roots and white communicating rami of the thoracic and lumbar nerves. The chemical mediator of the postganglionic fibers of the sympathetic system is norepinephrine, which is also produced by the adrenal medulla, and the nerve fibers are termed adrenergic fibers. Cells of adrenal medulla secrete adrenalin and nor adrenalin in response to preganglionic sympathetic stimulation. (The adrenal medulla is the only organ that receives preganglionic fibers, because nearly all the cells, after migration to the gland, differentiate into secretory cells.

The parasympathetic system

The parasympathetic system has its nuclei in the medulla and midbrain and in the sacral portion of the spinal cord. The preganglionic fibers of these neurons leave through four of the cranial nerves (III, VII, IX, and X) and also through the second, third, and fourth sacral spinal nerves. The parasympathetic system is therefore also called the craniosacral division of the autonomic system. The second neuron of the parasympathetic series is found in ganglia smaller than those of the sympathetic system; it is always located near or within the effector organs. These neurons are usually located in the walls of organs (e.g., stomach, intestines), in which case the preganglionic fibers enter the organs and form a synapse there with the second neuron in the chain.

The chemical mediator released by the pre- and postganglionic nerve endings of the parasympathetic system, **acetylcholine,** is readily inactivated by acetylcholinesterase—one of the reasons parasympathetic stimulation has both a more discrete and a more localized action than does sympathetic stimulation.

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***Peripheral Nervous System***

The peripheral nervous system PNS, consists of ***nerves, ganglia, and nerve endings***. The ganglia are nodular masses of neuronal cell bodies (ganglion cells), together with their supporting peripheral neuroglia, ***capsule cells*** or ***satellite cells***. There are two kinds of ganglia in the PNS- ***sensory ganglia*** which contain cell bodies of sensory (afferent neuron), and ***autonomic ganglia***, which contain cell bodies of certain efferent neurons of the autonomic nervous system. The sensory ganglia include the ***cranial ganglia***, which are associated with some of the cranial nerves, and the ***spinal ganglia***, known as posterior (dorsal) root ganglia, which are associated with posterior root of the spinal nerves.

Peripheral nerves consist of bundles of nerve fibers (myelinated and unmyelinated). Afferent fibers and efferent fibers are both present in most nerves. Afferent nerve endings are a part of sensory receptors, and efferent nerve endings are found on muscle fibers, secretory cells of exocrine glands, and fat cells of adipose tissue.

***Ganglia***

***Spinal ganglia***

Ganglion cells have the typical features of neurons, i.e. large rounded cell body, intense cytoplasmic basophilia with fine Nissl bodies, The nucleus is large spherical pale staining with prominent nucleolus (owl’s eye appearance), and is centrally located. Lipofuscin pigment may be present in the cytoplasm. A layer of flat capsule cells or satellite cells invest the cell body. The satellite cells are the neuroglial cells in the peripheral nervous system. The ganglion cells and the satellite cells are both derived from the neural crest and are supported by connective tissue framework and a capsule.

The ganglion cells are pseudounipolar neurons, therefore in a tissue sections they appear as rounded because the processe was not in the plane of the section.

***Autonomic Ganglia***

Autonimc ganglia are bulbous dilatations appear in the autonomic nerves. Some are located within certain organs, especially in the walls of the digestive tract, where they constitute the intramural ganglia. In autonomic ganglia the margins of the ganglion cells are indistinct because they are multipolar. The cytoplasm is basophilic with fine Nissl granules with eccentrically situated nucleus. The satellite cells are discontinuous unlike their counterpart of the spinal ganglia. The nucleus of the ganglion cell bodies has an eccentric position. The connective tissue capsule is not prominent

***Peripheral nerves***

The peripheral nerves are tough and resilient. They have a whitish, homogeneous, glistening appearance because of their myelin and collagen content. Nerves have an external fibrous coat of dense connective tissue called **epineurium,** which also fills the space between the bundles of nerve fibers. Each bundle is surrounded by the **perineurium,** a sleeve formed by layers of flattened epitheliumlike cells. The cells of each layer of the perineurial sleeve are joined at their edges by tight junctions, an arrangement that makes the perineurium a barrier to the passage of most macromolecules and has the important function of protecting the nerve fibers from aggression. Within the perineurial sheath run the Schwann cell-sheathed axons and their enveloping connective tissue, the **endoneurium**. The endoneurium consists of a thin layer of reticular fibers, produced by Schwann cells.

***Nerve Endings (Receptors)***

Nerve receptors are distributed throughout the body, mainly in the skin. Two types of nerve endings have been identified

* ***Free Nerve Endings***
* ***Encapsulated Nerve Endings***

***Free Nerve Endings***

Free nerve endings are situated in the deeper layer of the epidermis and in the papillary layer of the dermis. They are supplied with afferent nerve endings that are free of investing Schwann cells. They are ***sthermoreceptor,*** ***nociceptors*** and ***the mechanoreceptors*** that are related to the hair follicles

Encapsulated Nerve Endings

These are:

* Pacinian Corpuscles
* Meissners Corpuscles
* Ruffini Corpuscle
* Krause end bulb

***Pacinian Corpuscles*** are the largest encapsulated receptors; they are pressure-sensitive mechanoreceptors, present in joints and the pancreas. They are easy to recognize in sections as they are similar to onion bulbs. The afferent nerve ending is surrounded by multiple concentric layers of flat cells (regarded as modified Schwann cells) and the corpuscle is invested by a strong connective tissue capsule.

***Meissner’s corpuscles*** are for touch sensitivity and are highly sensitive. They are best observed in the dermal papillae, composed of flat cells (modified Shwann cells) lie transversely in the corpuscle, parallel to the skin surface. Helical terminal branches of several afferent nerve fibers lie with the cells and a connective tissue capsule invests the whole corpuscle.