# INTRODUCTION

Cerebral protection refers to relative preservation of neuronal structure and function, it implies a reduction in the rate of neuronal loss over time. Cerebral protection aims to prevent or slow disease progression and secondary injuries by halting or at least slowing the loss of neurons. **(Seidl and Potashkin, 2011; Casson et al., 2012).**

The brain has a high energy requirement, utilizing about 3-5 ml $O_2$/min/100 gm tissue and 5 mg glucose/min /100 gm tissue. The ability of brain to store precursors of metabolism is very little, so it depends on a constant supply of nutrient from blood. At cerebral blood flow of 50 ml/min /100 gm tissue and normal blood content of oxygen (20 ml $O_2$/100 ml blood), the brain receives 2-3 times the amount needed of oxygen, and at blood glucose concentration 70-110 mg/100 ml blood, the brain receives 10 times the amount of glucose that it needs. **(Heaviside and Hayes, 2009).**

Neurons are extremely sensitive to any impairment in substrate delivery, especially oxygen and glucose deprivation, which represents one of leading causes of irreversible brain damage. **(Mortier et al., 2000).**

Similarities in the pathogenesis of cerebral injuries may indicate that, protective and therapeutic strategies following

ischemia also are beneficial after trauma. **(Bramlett and Dalton 2004).**

Cerebral ischemic injury is directly proportional to the duration and extent of interrupted nutrient delivery; outcome can be improved simply by reducing the period of insult. **(Wass and Lanier, 1998).**

# AIM OF THE STUDY

The aim of this essay is to discuss the pathophysiology of different cerebral injuries, the strategies of cerebral protection and the candidates for cerebral protection in intensive care units.

# CEREBRAL ANATOMY AND PHYSIOLOGY

## Cerebral anatomy

The brain lies in the cranial cavity continuous with the spinal cord through the foramen magnum. It is surrounded by three meninges, the dura mater, the arachnoid mater and the pia mater, these are continuous with the corresponding meninges of the spinal cord. The cerebrospinal fluid surrounds the brain in the subarachnoid space. **(Snell, 2010).**

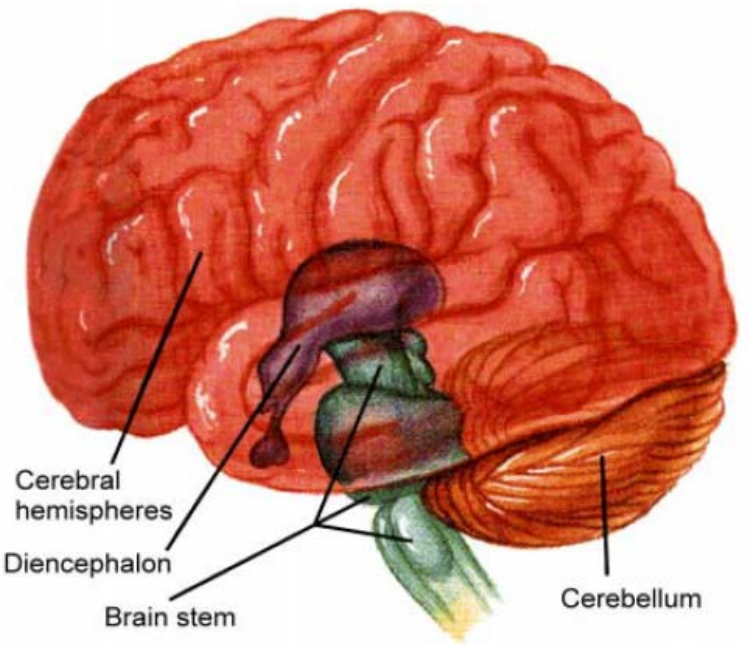


**Fig. 1:** Gross anatomy of brain**. (Williams, 2001).**

On a functional basis, the brain may be pictured as being made up of four major divisions (fig.1):

1- Brainstem which comprising from below upward the medulla oblongata, Pons and midbrain.

2- Cerebellum.

3- Diencephalon which comprising mainly, the thalamus and hypothalamus.

4- Cerebral hemispheres. **(Ellis and Mahadevan, 2013).**

## 1- Brainstem:

The brainstem is the most caudal part of the brain, connects the forebrain and cerebellum to the spinal cord. It consists of three main regions; the midbrain is the most rostral portion, which connects the forebrain to the pons; the middle portion, which connects to the cerebellum and the medulla oblongata, the most caudal portion, which connects to the spinal cord. The brainstem contains many nuclei that perform a wide variety of functions. Within the brainstem are processing centers for 10 of the 12 pairs of cranial nerves, peripheral nerves that emanate directly from the brain rather than the spinal cord. Also located within the brainstem is the reticular formation, a diffuse network of nuclei that plays important roles in sleep-wake cycles, arousal of the cerebral cortex, and consciousness. In

addition, the brainstem is important in the regulation of many involuntary functions controlled by the autonomic nervous system, such as cardiovascular function and respiratory function. **(Stanfiled, 2013).**

## 2- Cerebellum:

The cerebellum occupies about 10% of the brain volume but contains more neurons than the entire rest of the brain. The cerebellum is divided into the 3 functional divisions of the spinocerebellum, cerebrocerebellum, and flocculonodular lobe. Each division in the cerebellar cortex sends Purkinje cell axons to specific deep cerebellar nuclei and has different functions. Cerebellar neurons do not directly produce motor movements, but act more as a comparator that compensates for errors in movement by comparing intention with performance and making subtle adjustments. As such, patients with cerebellar diseases do not have weakness or sensory loss. **(Davis et al., 2005).**

## 3- Diencephalon:

The diencephalon consists of the thalamus, hypothalamus, optic nerves, pituitary gland, and pineal gland. The thalamus is critical for the relay, gating, and integration of information that reaches the cerebral cortex. Through connections with the cerebral cortex, brainstem, pituitary, and pineal gland, the

hypothalamus is important in the control of circadian rhythms, the sleep-wake cycle, homeostasis, and reproduction. The visual system, a derivative of the diencephalon, provides input to the cerebral cortex for the identification of objects and motor control under visual guidance. **(Benrracho et al., 2008).**

## 4- Cerebral hemispheres:

The hemispheres can each be divided into four major lobes. The frontal lobes lie over the orbital bones and are responsible for thinking, voluntary eye movements, mature judgments and self control. They are separated from the more posterior parietal lobes by a vertical groove called the central sulcus, and the strip of frontal cortex running just anterior to the sulcus is the primary motor control centre and controls the contralateral side of body. The primary sensory cortex exists on the strip of parietal cortex just posterior to the sulcus, and is responsible for discerning fine touch, determining proprioception, pain and temperature. The area around the most posterior tip of the brain, occipital lobe is the visual cortex, responsible for the interpretation of sight and for high level control of the occulomotor complex. Extending forward and laterally is the temporal lobe, whose deeper structures form the limbic systems that play important roles in memory and learning. **(Williams, 2001).**

## Protective Covering of the Brain

The first layer of protection for the central nervous system is the hard bony skull. The skull encases the brain, providing strong protective defenses against damaging blows or bumps. The second protective layer is the meninges, three membranes that lie between the bony encasement and the nervous tissue of the brain. Finally, a space between two of the meningeal membranes contains cerebrospinal fluid (CSF), a buoyant liquid that suspends the nervous tissue in a weightless environment while surrounding it with a shock absorbing, hydraulic cushion. **(Tortora and Derrickson, 2014).**

Three concentrically arranged membranes, known as meninges, surround the brain. From outside in, these three layers are the *dura* mater, *arachnoid* mater and *pia* mater.

The *dura* is a dense membrane which, within the cranium, is often described as being made up of two layers. The outer layer of the dura is intimately adherent to the inner surface of the skull; the inner layer is fused with the outer layer except where the two layers are separated by the intracranial dural venous sinuses and where the inner layer projects inwards to form four, prominent, reduplicated sheets, the falx cerebri; the falx cerebelli; the tentorium cerebelli and the diaphragma sellae.

The *arachnoid* is a delicate membrane applied, throughout, to the inner surface of the dura, and separated from the dura by the potential *subdural* space.

The *pia* is closely moulded to the surface of the brain; it dips down into all the cerebral sulci. The interval between the pia mater and the overlying arachnoid is termed the *subarachnoid* space. This space contains cerebrospinal fluid and is traversed by trabeculae of fine fibrous strands that run from the arachnoid to the pia. **(Ellis and Mahadevan 2013).**

**Cerebral ventricles and cerebrospinal fluid:**

The fluid filled cerebral ventricles constitute the inner CSF space. Each of the two lateral ventricles communicates with the third ventricle through the interventricular foramen of Monro (one on each side). Fluid passes from the third ventricle through the cerebral aqueduct of Sylvius into the fourth ventricle and then through the single midline foramen of Magendie and paired lateral foramina of Luschka into the subarachnoid space; outer CSF space, (fig.2). **(Ellis and Mahadevan, 2013).**

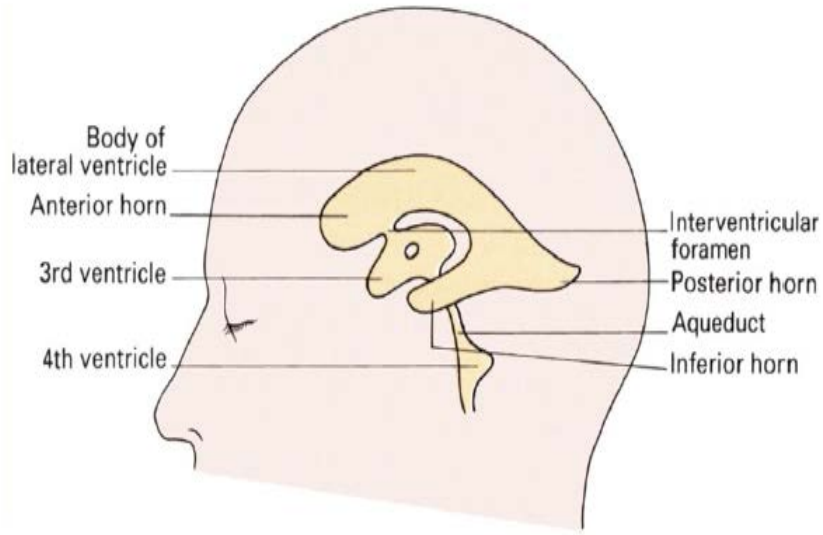


**Fig.** 2**:** The ventricular system (**Ellis and Mahadevan, 2013).**

The CSF, a clear and colorless ultra filtrate of blood plasma, is mainly produced in the choroid plexus of the cerebral ventricles and in the capillaries of the brain. Its functions are both physical; compensation for volume changes, buffering and equal distribution of intracranial pressure despite variation in venous and arterial blood pressure and metabolic; transport of nutrients and hormones into the brain, and of waste products out of it. **(Rohkamn, 2003).**

## Arterial supply to brain:

The brain receives 15-20%of the blood pumped by the heart under resting conditions. This large blood supply is necessary because brain has a high rate of metabolic activity compared to most other tissues and, therefore, has a high demand

for glucose and oxygen to meet its energy needs. Under resting conditions, the brain accounts for 20% of all oxygen that the body consumes, and 50% of all glucose consumed. To ensure delivery of these needed materials, adequate blood flow to brain must be maintained at all times. In fact, brain is so dependent on this blood supply that disruption of blood flow for even a few minutes can result in irreversible damage to brain. **(Standfiled, 2013).**

The cerebral circulation is divided into two parts. The anterior circulation is fed by the internal carotid arteries, while the posterior circulation derives from the vertebral arteries. **(Macfarlane, 2000).**

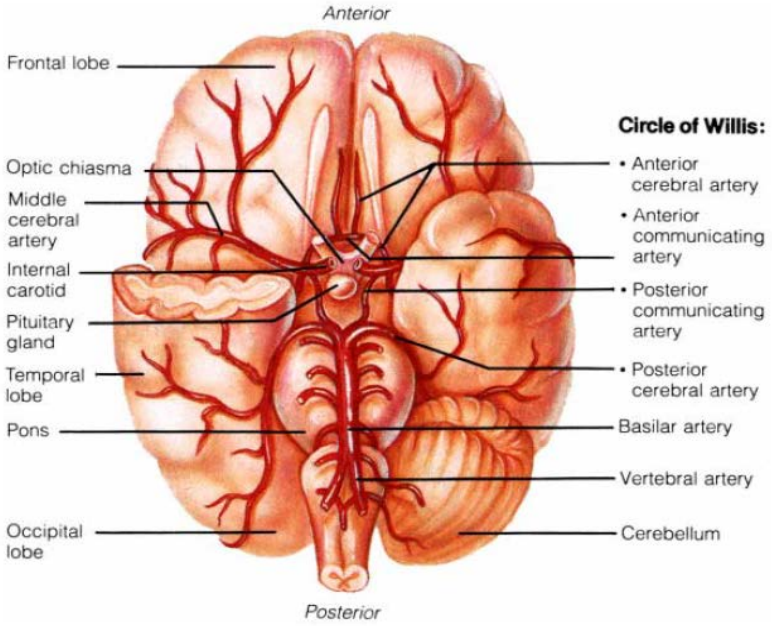


**Fig.** 3**:** Anatomy of the Circle of Willis **(Burnstein, 2001).**

The blood supply to the forebrain is derived from the both internal carotid arteries and the basilar artery, while brain stem and cerebellum are supplied by vertebral and basilar arteries. These arteries form anastomosis at base of brain called circle of Willis (fig.3), which comprises the anterior communicating artery, both anterior cerebral arteries, both internal carotids, both posterior communicating arteries and posterior cerebral arteries. **(McCaffrey, 2002)**.

## Venous drainage of the brain:

The cerebral hemispheres are drained by superficial and deep cerebral veins. Superficial cerebral veins drained into dural venous sinuses. The deep cerebral veins unit as great cerebral vein and drained into straight sinus. The cerebellar veins are placed on the surface of cerebellum, and are disposed in two sets; superior and inferior. The sinuses drained into internal jugular, which is continuous with sigmoid sinus. **(Ellis and Mahadevan, 2013).**

## Microcirculation:

The architecture of the cerebral microvasculature is highly organized. Pial vessels on the surface of the brain give rise to arterioles that penetrate the brain at right angles. These arterioles give rise to capillaries at all laminar levels. Each arteriole supplies a hexagonal column of tissue, with overlapping

boundary zones resulting in columnar patterns of local blood flow. This parallels the columnar arrangement seen within neuronal groups and physiologic functional units. Capillary density in adults is related to the number of synapses and can be closely correlated with the regional level of oxidative metabolism. **(Burnstein and Yarham, 2008).**

# Cerebral physiology

## Physiology of cerebral circulation:

The adult brain (1200–1400 g) comprises 2–3% of total body weight and receives 15–20% of cardiac output. The central nervous system has a high metabolic rate for oxygen ($CMRO_2$) and uses glucose predominantly as the substrate for its energy needs. Although glial cells make up almost 50% of the brain, they consume less than 10% of total cerebral energy due to their low metabolic rate. Neurons expend most of the available energy. 50% of the total energy generated is used for maintenance and restoration of ion gradients across the cell membrane, and the remaining 25% is used for molecular transport, synaptic transmission and other processes. **(Torbey and Bhardwaj, 2004).**

The whole brain oxygen ($O_2$) consumption is approximately 3-5 ml of oxygen / 100 g of brain tissue / min. The substantial demands for both oxygen and glucose are met by maintaining cerebral blood flow (CBF). CBF is related to cerebral perfusion pressure (CPP) and cerebrovascular resistance (CVR) as follows: CBF = CPP / CVR, where CPP = Mean arterial pressure (MAP) – Intracranial pressure (ICP) – venous pressure (VP). **(Prabbu and Gupta, 2001).**

Cerebral autoregulation is defined as the relationship between CBF and CPP. Complex neurohumoral processes are involved in myogenic and metabolic mechanisms to maintain CBF at a constant level in the presence of fluctuating systemic and cerebral perfusion pressures. **(Myburgh, 2004).**

## Myogenic autoregulation:

Myogenic autoregulation is the term used to describe changes in cerebrovascular transmural pressure in response to fluctuations in MAP. This is mediated through adrenergic stimulation of vascular smooth muscle and microfluxes of endogenous vasodilators (e.g. nitric oxide) and vasoconstrictors (e.g. endothelin). In cerebrovascular terms, myogenic autoregulation is regarded as the relationship between CBF and CPP. Under physiological conditions, CBF is maintained at a constant rate until autoregulatory thresholds are exceeded and CBF becomes "pressure passive". The "break points" where this occurs vary considerably between individuals, but is traditionally recorded as 60 and 160 mmHg. **(Myburgh, 2004).**

## Metabolic autoregulation:

Metabolic autoregulation is the term used to define non myogenic mechanisms of cerebral vasoregulation. Of these, reactivity of the cerebral vasculature to systemic and local changes in arterial carbon dioxide tensions ($PaCO_2$) is regarded as the basis of metabolic autoregulation. Under physiological