**QUESTION 1: PHYSIOLOGY OF SLEEP**

Sleep is the natural periodic state of rest for mind and body with closed eyes characterized by partial or complete loss of consciousness.

Sleep requirements: New born infants: 18 to 20 hours; Growing children: 12 to 14 hours; Adults: 7 to 9 hours; Old persons: 5 to 7 hours.

The **physiology of sleep** is characterized by two phases

* Rapid eye movement sleep (REM)
* Non-rapid eye movement sleep (NoREM)
* Rapid eye movement sleep or REM: this is associated with rapid conjugate movements of the eyeballs, which occurs frequently. Though the eyeballs move, the sleep is deep. So, it is also called paradoxical sleep. It occupies about 20% to 30% of sleeping period. Functionally, REM sleep is very important because, it plays an important role in consolidation of memory. Dreams occur during this period.
* Non-rapid eye movement sleep or NREM: this is the type of sleep without the movement of the eyeballs. Also called slow-wave sleep. Dreams do not occur hear. It occupies about 70% to 80% of total sleeping period. Non-REM sleep is followed by REM sleep.

**Stages of the sleep**

There are 4 phases of the non-REM sleep (NREM) sleep process and another of REM sleep.

**NREM phase**

**Stage NREM- Phase1:** It is the stage where we feel drowsy or we are asleep. The waking state is disappearing since the Alpha rhythm also does it. At the moment, muscle tone does not relax completely. The Beta waves have disappeared. EEG shows only low voltage fluctuations and infrequent delta waves.

**Stage NREM- Phase II-III (Light to Medium sleep)**

**Phase 2** is characterized by spindle bursts at a frequency of 14 per second, superimposed by low voltage delta waves.It is the stage where although we are asleep, the dream is light, the Alpha rhythm disappears more and more, muscle tone continues to exist.

**Phase 3: stage of medium sleep**: during this stage, the spindle bursts disappear. Frequency of delta waves decreases to 1 or 2 per second and amplitude increases to about 100uv. We experience the entrance to the theta waves little by little.

**Stage NREM- Phase IV**

This is the stage of deep sleep, the encephalographic rhythm is very low, muscle tone is maintained or may be greatly diminished. Delta waves appear in our brain with low frequency and high amplitude.

Actually these stages differ in that the muscular atony is gradually increased and brain waves are gradually changing depending on the relaxation of the body.

**REM phase**

This is the paradoxical dream phase, since during this phase the brain has an activity that resembles that which occurs when we are awake. Also during this phase rapid eye movements are seen. The body is in atony. electroencephalogram (EEG) shows desynchronized waves i.e an irregular wave with high frequency and low amplitude.

**How is sleep organized during the night?**

Adults usually have about 8 hours of sleep per day. If the 8 hours are carried out in a continuous manner, it will take about 4 or 5 cycles. Each cycle can be understood as complete phases of sleep (from stage I to REM phase), and can last between 90 and 120 minutes each.

The distribution is usually the following:

* Phase I during the cycle would be developing approximately 1.5% of the total cycle. This means that if the cycle lasts 100 minutes, only 1 minute and a half the body would be in phase I.
* Phase II during the cycle would be present approximately 25% of the total cycle. In a cycle of 100 minutes, 25 minutes would be the duration of Phase II.
* Phase III and IV during the cycle would last 45% of the total cycle. In a 100-minute cycle, these phases would last approximately 45 minutes.
* The REM phase, during the cycle would have a duration of 25% of the total cycle. So in a cycle of 100 minutes, only 25 minutes correspond to the paradoxical dream and dreams.

**Physiological changes during sleep**

* Tone in all the muscles of body except ocular muscles decreases very much during sleep.
* Brain is not inactive during sleep. There is a characteristic cycle of brain wave activity during sleep with irregular intervals of dreams.
* Plasma volume decreases by about 10% during sleep.
* Rate and force of respiration are decreased.
* Salivary secretion decreases during sleep. Gastric secretion is not altered. Contraction of empty stomach is more vigorous
* Sweat secretion increases during sleep.
* Lacrimal secretion decreases during sleep.
* Heart rate reduces. It varies between 45 and 60 beats per minute.
* Systolic pressure falls to about 90 to 110 mm Hg.
* Certain reflexes particularly knee jerk, are abolished. Threshold for most of the reflexes increases. Pupils are constricted.

**The Dream Is Governed by A Biological Clock**

The sleep process is governed by a biological rhythm understood as circadian rhythm. These are 24-hour cycles that are related to day and night.

The circadian rhythm of sleep and wakefulness is approximately every 25 hours. This data is curious because this tells us that we are programmed in such a way that we allow ourselves to be influenced by a certain rhythm or cycle.

In our central nervous system there is one of our biological clocks. This watch makes non-REM sleep and REM sleep last a certain time.

Circadian rhythms depend on the interaction of the organism with the stimuli that come from outside. Of these external stimuli the most important and the one that most influences us is light, as well as the time to wake up, since this time can be fixed strictly.

The time we go to sleep is also important, and although we can set a routine guideline that make us at a certain time we are in bed, we cannot usually decide the exact moment in which we fall asleep.

If the person is totally isolated from these stimuli, that is, he does not perceive changes of light, temperature, activities, etc … he would also follow a normal biological rhythm of sleep, since the human body is programmed to follow the rhythm we need without need for external influences.

Sleep occurs due to the activity of some sleep-inducing centres in brain. Stimulation of these centres results in sleeplessness or persistent wakefulness called insomnia.

* Applied physiology-sleep disorders
* Insomnia: this is the inability to sleep or abnormal wakefulness. It is the most common sleep disorder. It occurs due to systemic illness or mental conditions such as psychiatric problems, alcohol addiction and drug addiction.
* Hypersomnia: this is the excess sleep or excess need to sleep. It occurs because of lesion in the floor of the third ventricle, brain tumours, encephalitis, chronic bronchitis and disease of muscles. Hypersomnia also occurs in endocrine disorders such as myxoedema and diabetes insipidus.
* Nightmare: this is a condition during sleep that is characterised by a sense of extreme uneasiness or discomfort or by frightful dreams. It occurs mostly during REM sleep. Nightmare occurs due to improper food intake, digestive disorders or nervous disorders. It also occurs during drug withdrawal or alcohol withdrawal.

**QUESTION 2: THE BASAL GANGLIA AND ITS ROLE IN MOVEMENT**

Regulation of voluntary movement: movements during voluntary motor activity are initiated by cerebral cortex. However, these movements are controlled by basal ganglia, which are in close association with cerebral cortex. During lesions of basal ganglia, the control mechanism is lost and so the movements become inaccurate and awkward. Basal ganglia control the motor activities because of the nervous circuits between basal ganglia and other parts of the brain involved in motor activity. Neuronal circuits arise from three areas of the cerebral cortex:

* Premotor area
* Primary motor area
* Supplementary motor area

All these nerve fibres from cerebral cortex reach the caudate nucleus. From here, the fibres go to putamen. Some of the fibres from cerebral cortex go directly to putamen also. Putamen sends fibres to Globus pallidus. Fibres from here run towards the thalamus, subthalamic nucleus of Luys and substantia nigra are in turn, projected into thalamus. Now, the fibres from thalamus are projected back into primary motor area and other two motor areas, i.e. premotor area and supplementary motor area.

Regulation of conscious movements: Fibres between cerebral cortex and caudate nucleus are concerned with regulation of conscious movements. This function of basal ganglia is also known as cognitive control of activity. For example, when a stray dog barks at a man, immediately the person, understands the situation, turns away and start running.

Regulation of subconscious movements: Cortical fibres reaching putamen are directly concerned with regulation of some subconscious movements, which take place during trained motor activities, i.e. skilled activities such as writing the learnt alphabet, paper cutting, nail hammering, etc.

The basal ganglia are a collection of subcortical structures consisting of several connected nuclei located in the brain. They are called the caudate nucleus, putamen, globus pallidus, subthalamic nucleus, and substantia nigra (the last two are only functionally connected and related to this system). Three major pathways emerge from the basal ganglia, which project onto various structures of the brain, communicating with them. They are called the **direct** (excitatory), **indirect** (inhibitory) and **hyperdirect** (inhibitory) pathways. Their activity is modulated by D1 and D2 dopamine receptors contained in the substantia nigra, pars compacta.

**DIRECT PATHWAY**

The direct pathway starts from the cortex and projects to the **striatum** (caudate nucleus and putamen) with excitatory glutamatergic (glu) neurons. The neurons from the striatum, which are inhibitory GABAergic, send their axons to the medial (internal) globus pallidus and substantia nigra, pars reticulata (SNr).

The neurons from the internal globus pallidus and SNr send their axons to the **thalamus**, and they are also inhibitory. The fibers that travel from the pallidum to the thalamus, form two white matter fascicles called ansa lenticularis and lenticular fasciculus, that fuse into one pathway called thalamic fasciculus just before they enter the thalamus. From the thalamus, excitatory pathways go to the **cortex** (prefrontal, premotor and supplementary cortex) where they affect the planning of the movement by synapsing with the neurons of the corticospinal and corticobulbar tracts in the brainstem and spinal cord.

This entire system functions on the principle of **positive feedback**. Since the two of the inhibitory synapses are serially connected, that means that the first inhibitory neuron (striatum) suppresses the activity of the second inhibitory neuron (globus pallidus). The result of this is a reduction of the inhibitory influence that the globus pallidus has over the thalamus, so-called **disinhibition of the thalamus**, which is equivalent to the excitation of the motor cortex. So the final function of the direct pathway of the basal ganglia is to excite the motor cortex or to increase the motor activity.

**INDIRECT PATHWAY**

This pathway begins (like the direct pathway) from the cortex, projecting to the **striatum**. Instead of sending axons directly to the GPi and SNr, they project to the external globus pallidus GPe.

The neurons from the GPe send inhibitory fibers to the **subthalamic nucleus** instead of sending directly to the thalamus (hence its name “indirect”). From the subthalamic nucleus, neurons send their axons to the GPi/SNr and then continue as the direct pathway with GABAergic inhibitory neurons to the thalamus and glutamate excitatory efferents to the cortex.

So, functionally, the striatum inhibits the external globus pallidus, and that causes **disinhibition of the subthalamus**. For that reason, the neurons of the subthalamus become more active, and they excite the internal segment of the globus pallidus which in the end, inhibits the thalamic nuclei. The final result of this pathway is a decreased activity of the cortical motor neurons and consequential **suppression** of the extemporaneous movement.

The hyperdirect pathway is a dopaminergic pathway, nigostriatal pathway. Pars compacta in substantia nigra release dopamine to the striatum activating D1 and D2 receptors in the striatum. D1 receptors stimulate the direct pathway while D2 receptors inhibit the indirect pathway. Therefore, both receptors will lead to an increase excitability of motor cortex and increase in motion. Damage to the substantia nigra leads to decreased motion, poor posture and tremors as seen in Parkinson’s disease.