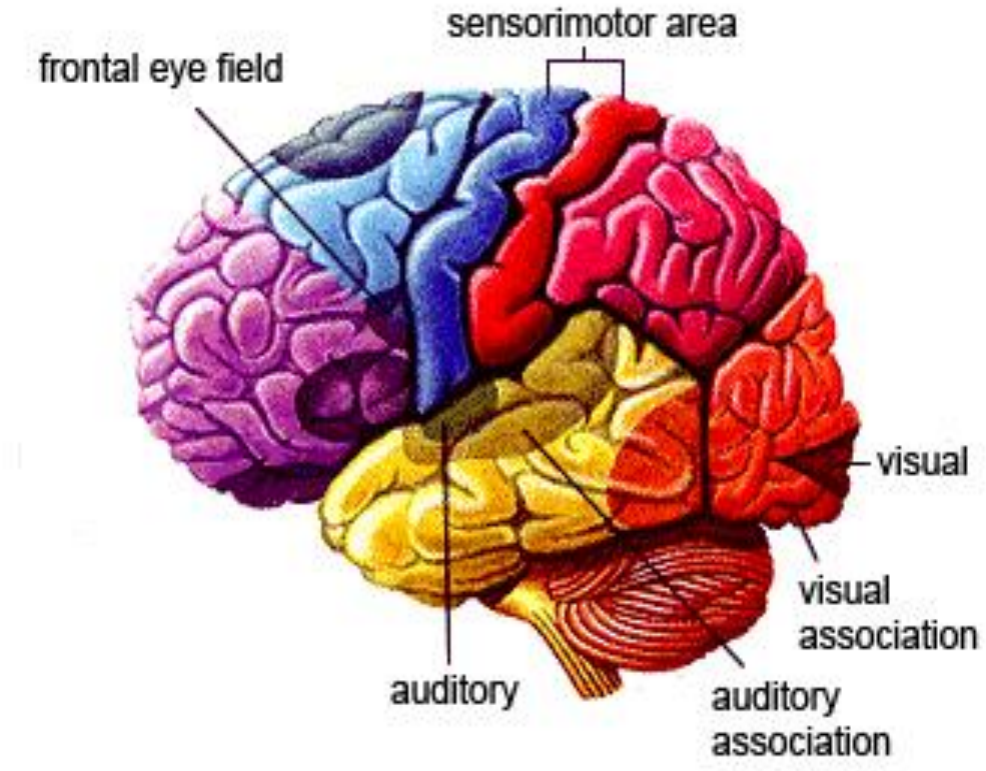
# Physiology Team




Amna Baljoun

Ahlam Al –Maawi

Areej Al Kahtani

Bodoor Al Tayeb

Asmaa` Bedawi

( these notes are combination of female and male slides + our notes )

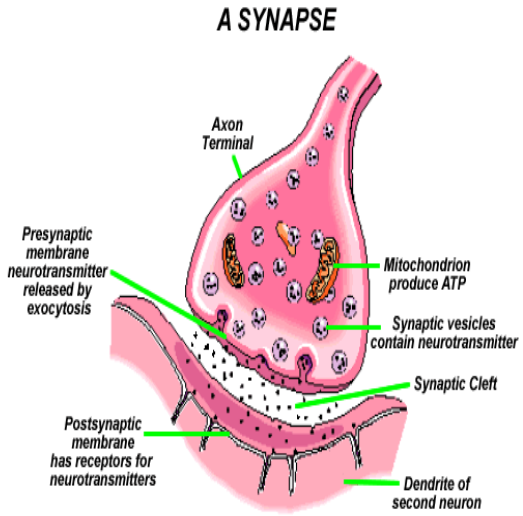
# Synapses and Synaptic Transmission

## INTRODUCTION TO SYNAPSE:

1. **The CNS contains more than 100 billion neurons.**
2. **Incoming signals enter the neuron through synapses located mostly on the neuronal dendrites, but also on the cell body.**
3. **For different types of neurons, there may be only a few hundred or as many as 200,000 such synaptic connections from input fibers.**
4. **Conversely, the output signal travels by way of a single axon leaving the neuron.**

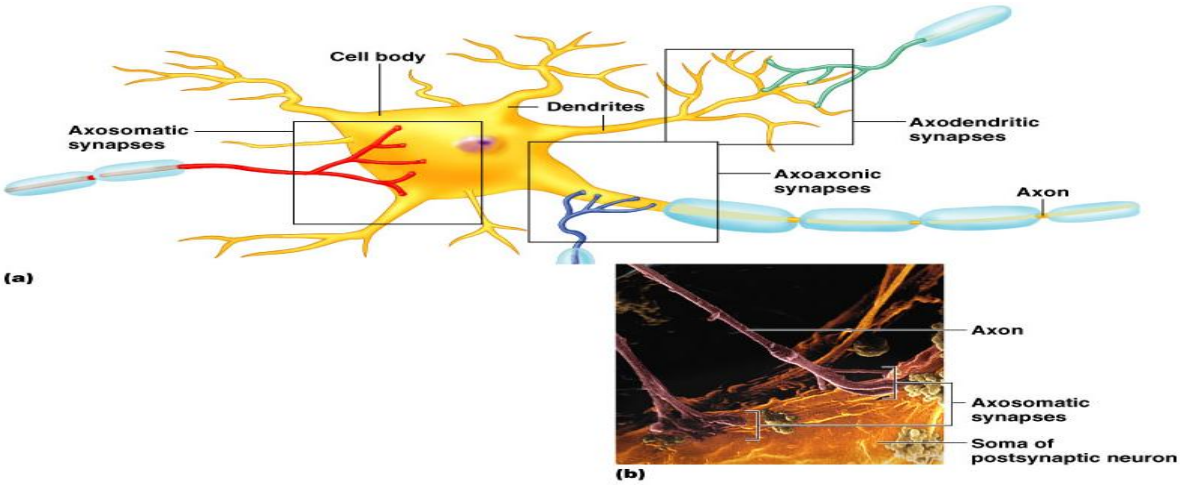
## SYNAPSE:

**A junction where the axon or some other portion of one cell (= presynaptic cell) terminates on the dendrites, soma, or axon of another neuron (post synaptic cell).**




## Anatomical Types of Synapses:

1. **Axodendritic (axon to dendrite)**
2. **Axosomatic (axon to soma)**
3. **Axoaxonic (axon to axon)**
4. **Dendrodendritic (dendrite to dendrite)**
5. **Dendrosomatic (dendrites to soma)**



## Types of synapses ( functional classification):

### A. Chemical synapse:

**Almost all synapses used for signal transmission in the CNS of human being are chemical synapses.**

**i.e. first neuron secretes a chemical substance called neurotransmitter at the synapse to act on receptor on the next neuron to excite it, inhibit or modify its sensitivity.**

### B. Electrical Synapses:

**Membranes of the pre- and post-synaptic neurons come close together and gap junctions forms → low membrane borders which allow passage of ions.**

- **Are less common than chemical synapses**
- **Correspond to gap junctions found in other cell types**
- **Are important in the CNS in:**
  - **Arousal from sleep**
  - **Mental attention**
  - **Emotions and memory**
  - **Ion and water homeostasis**

### B. Conjoint synapse:

- **Both electrical and chemical.**
- **Examples → neurons in lateral vestibular nucleus.**

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## What happens at the synapse?

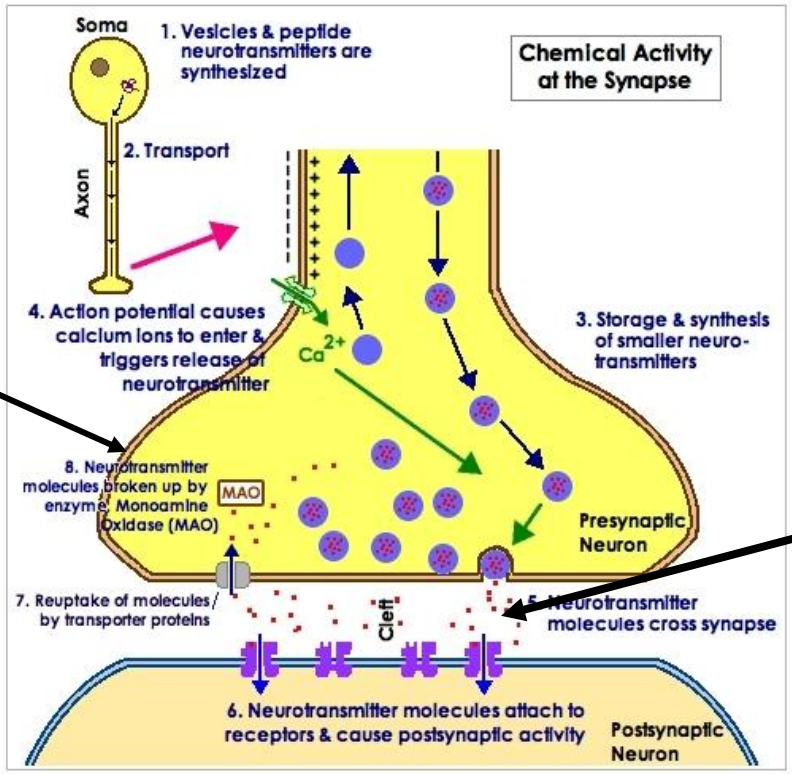
**Information is transmitted in the CNS mainly in the form of APs "=nerve impulse", which pass from one neuron to another.**

**Each impulse from its way from one neuron to another may:-**

1. **Be blocked in its transmission from one neuron to another**
2. **Be changed from single impulse to repetititve impulses.**

**∴ Synaptic transmission is a complex process that permits grading and adjustment of neural activity necessary for normal function.**

**Synaptic knobs (presynaptic terminal )**




**Synaptic cleft:**

This the space between the axon terminal and sarcolemma.

## Postsynaptic neurons:

- **the membrane of post-synaptic neuron contains large number of receptor proteins.**

**Examples of synapses outside CNS:**

1. **NMJ**
2. **Contact between autonomic neurons smooth and cardiac muscles, and other effector cells.**

## Types of these receptors

Binding site that face the cleft to bind the neurotransmitter

. Ionophore: It passes all the way through the membrane to the interior. It is of two types

**Ion channels**

**Cation channels:**

Na+ (most common)

K+ , Ca++

Opening of Na+ channels

→ ↑ membrane potential

→ (+) neuron

**Anion channels:**

$Cl^-$ (mainly)

Opening of $Cl^-$ channels

→ ↓ membrane potential

→ (-) neuron

**2nd messenger system:**

in the post-synaptic membrane.

This mechanism is important for (memory).

**Its mechanism:**

**Opening of ion channel [open for prolonged time] → Activation of cAMP → long-term changes [memory] →Activation of intracellular enzymes → Activate gene transcription → protein + structural changes [memory] long-term memory .**

- **Most common type of 2nd messenger in neurons is G-protein**

## Fate of neurotransmitter:

- **Diffusion out of synaptic cleft into surrounding fluid**
- **Enzymatic destruction e.g. Ach esterase for Ach**
- **Active transport back into pre-synaptic terminal itself e.g. norepinephrine**

## . RMP of neuronal soma:

- **≃ –65mV .**
- **If the voltage is less negative → the neuron is excitable**
- **Causes of RMP:**

1. **Leakage of K+ (high K+ permeability)**
2. **Large number of negative ions inside: proteins, phosphate**
3. **Excess pumping of Na+ out by Na+-K+ pump**

## Excitatory post-synaptic potential [EPSPs]:

**When excitatory neurotransmitter bind to its receptor on post-synaptic membrane → partial depolarization [↑ Na influx or Ca++ channels] of post-synaptic cell membrane → If this potential rises enough to threshold level → AP will develop and excite the neuron (central or neuronal summation)**

- **This summation will cause the membrane potential to increase from –65mV to –45mV.**
- **∴ EPSPs = +20mV which makes the membrane reach the firing level → AP develops at axon hillock.**

Discharge of single pre-synaptic terminal can never increase the neuronal potential from –65mV to –45mV.

### Characteristics of EPSPs are:

- **Graded response**
- **Proportionate to the strength of the stimulus**
- **Can be summated**

- **How EPSP differs from AP?**
  - **They are proportional to the strength of the stimulus ( i.e., do not obey All-or-None Law)**
  - **They can summate ( add up )**

## Inhibitory post-synaptic potentials:

**localized increase in membrane permeability to $Cl^-$ of post-synaptic memb. (produced by inhibitory neurotransmitter) → ↓ excitability and memb. potential becomes away from firing level.**

**(hyperpolarization of the post-synaptic memb= IPSP).**

**IPSP = –5mV**

**EPSP= +20 mV**

**<u>Also IPSP can be produced by</u>:-**

- **Opening of K+ channels → outward movement of K+**
- **Closure of Na+ or Ca++ channels**

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## Synaptic properties:

### 1. One-way conduction:

**Synapses generally permit conduction of impulses in one-way i.e. from pre-synaptic to post-synaptic neuron.**

### 2-Synaptic delay:

**Is the minimum time required for transmission across the synapse.**

### 3.Synaptic inhibition:

**A. Direct inhibition.**

**B. Indirect inhibition.**

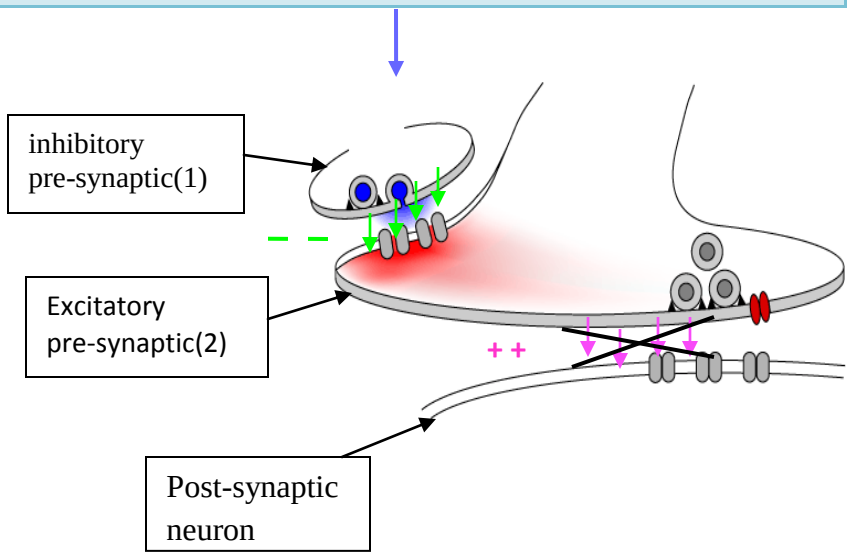
**C. Reciprocal inhibition.**

**D. Inhibitory interneuron.**

**E. Feed forward inhibition.**

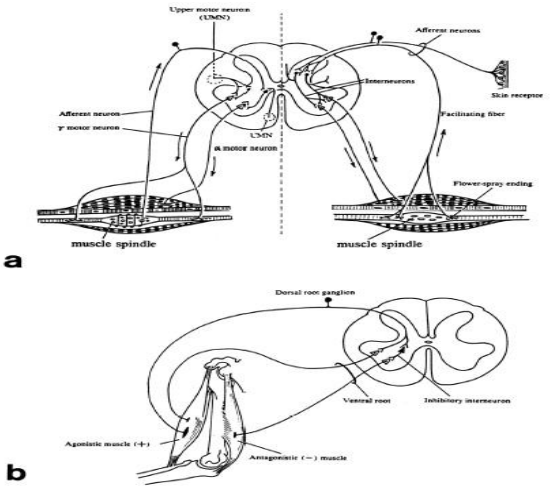
**F. Lateral inhibition.**

| Direct | Indirect |
| --- | --- |
| Post-synaptic inhibition.<br>Occurs when an inhibitory neuron [pre-synaptic neuron releasing inhibitory substance "neurotransmitter secreted is Glycine."] act on a post-synaptic neuron leading to its **hyperpolarization** due to opening of $Cl^-$ [IPSPs] and/or K+ channels. | Pre-synaptic inhibition.<br>This happens when an inhibitory pre-synaptic(1) fibers lie directly on the termination of a pre-synaptic(2) excitatory fiber.<br>The inhibitory pre-synaptic(1) fibers release a transmitter which inhibits the release of excitatory transmitter from the pre-synaptic(2) fiber.<br>The transmitter released is GABA.<br>The inhibition is produced by ↑ $Cl^-$ and ↑ K+. e.g. occurs in dorsal horn → pain gating. |

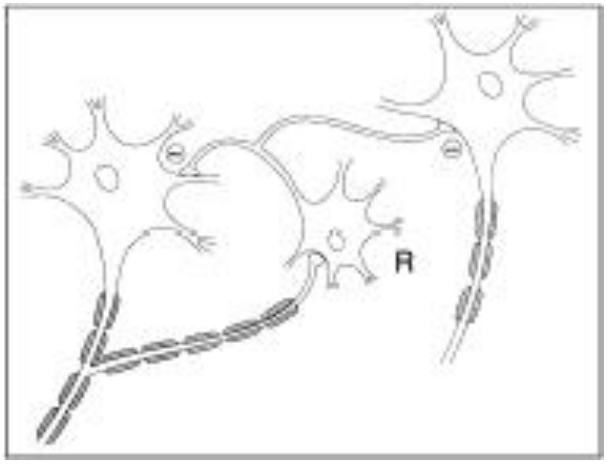



| Reciprocal | Interneuron ( Renshaw cells) |
| --- | --- |
| initiated in the spindle.<br>excitation in the agonist muscle and Inhibition of antagonist activity.<br>Impulses pass directly to the motor neurons supplying the same muscle and via branches to inhibitory interneurones that end on motor neurones of antagonist muscle. | Negative feedback inhibitory interneuron of a spinal motor neuron .<br>This feedback inhibition also occurs in: Cerebral cortex,Limbic system.<br><br>*Renshaw cells are in spinal cord. |

## Reciprocal inhibition:




## Interneuron inhibition:




### E. Feed forward inhibition:

**occurs in the cerebellum to limit the duration of excitation.**

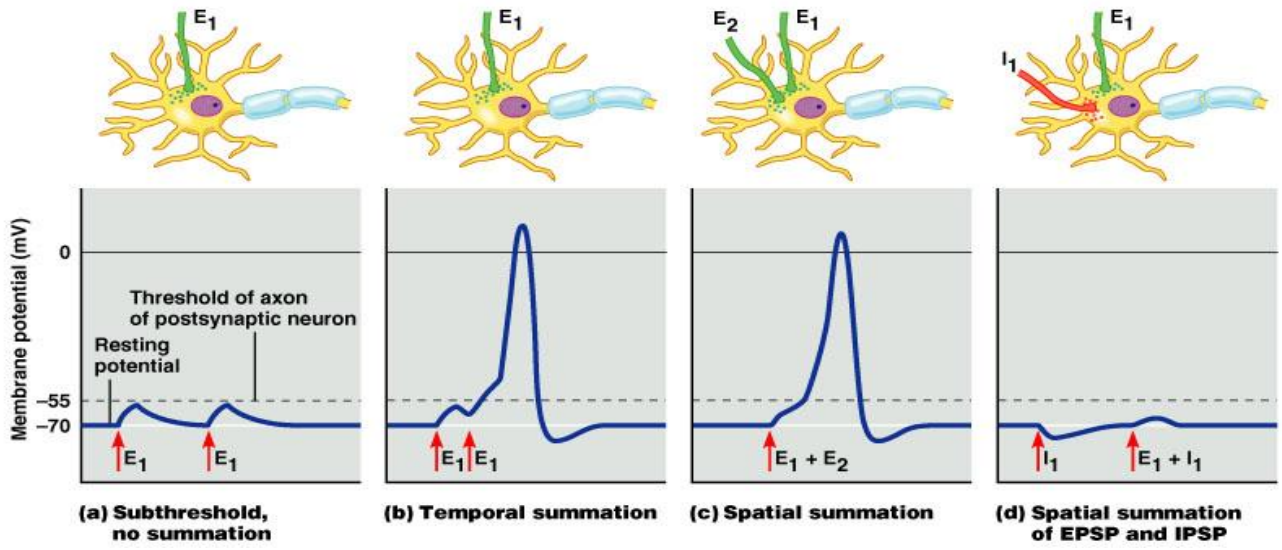
### F. Lateral inhibition:

**Because of lateral inhibition, the lateral pathways are inhibited more strongly. This happens in pathways utilizing most accurate localization. e.g. movement of skin hairs can be well located, temperature and pain are poorly located.**

## 4-Summation:

a) **Spatial summation:** **When EPSP occurs in more than one synaptic knob at same time.**

b) **Temporal summation:** **If EPSPs in a pre-synaptic knob are successively repeated without significant delay so the effect of the previous stimulus is summated to the next.**




## 5-Convergence and divergence:

**Convergence:** **When many pre-synaptic neurones converge on any single post-synaptic neuron.**

**Divergence:** **Axons of most pre-synaptic neurons divide into many branches that diverge to end on many post-synaptic neuron.**

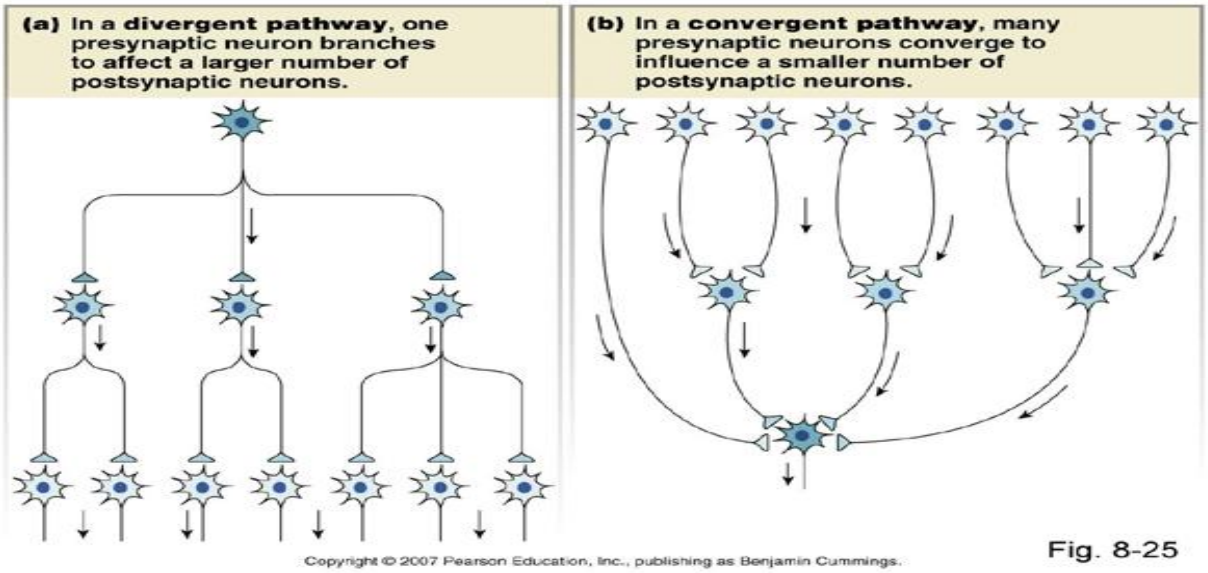





Fig. 8-25

## 6.Occlusion:

**↓ Expected response due to pre-synaptic fibers sharing post-synaptic neurone [=overlap].**

***Neuromodulation: non-synaptic action of a substance on neurons that alters their sensitivity to synaptic stimulation or inhibition. E.g. neuropeptides, steroids.**

## 7.Fatigue:

**Exhaustion of neurotransmitter.**

**If the pre synaptic neurons are continuously stimulated there may be an exhaustion of the neurotransmitter. Resulting in stoppage of synaptic transmission.**

## 8.Long-term potentiation (LTP):

**Rapidly developing persistent enhancement of post-synaptic potential response to pre-synaptic stimulation. After brief period of rapidly repeated stimulation of pre-synaptic neurone.**

**a) Increase Ca++ intracellular in post-synaptic membrane.**

**b) Increase Amygdala N-methyl-D-aspartate NMDA receptors.**

*** its related to memory.**

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# Factors affecting synaptic transmission:

## 1) Alkalosis:

**Normally, alkalosis greatly increases neuronal excitability.**

**For instance, a rise in arterial blood pH from the 7.4 norm to 7.8 to 8.0 often causes cerebral epileptic seizures because of increased excitability of some or all of the cerebral neurons.**

**This can be demonstrated especially well by asking a person who is predisposed to epileptic seizures to overbreathe.**

**The overbreathing blows off carbon dioxide and therefore elevates the pH of the blood momentarily.**

## 2) Acidosis:

**Conversely, acidosis greatly depresses neuronal activity.**

**A fall in pH from 7.4 to below 7.0 usually causes a comatose state.For instance, in very severe diabetic or uremic acidosis, coma virtually always develops.**

## 3) Drugs:

**Many drugs are known to increase the excitability of neurons, and others are known to decrease excitability.**

**For instance: Caffeine, Theophyline,**

**Theobromine, which are found in coffee, tea, and cocoa, respectively,**

**All *increase* neuronal excitability, presumably by reducing the threshold for excitation of neurons.**

**Strychnine is one of the best known of all agents that increase excitability of neurons.**

**However, it does not do this by reducing the threshold for excitation of the neurons; instead, it inhibits the action of some normally inhibitory transmitter substances.**

**especially the inhibitory effect of glycine in the spinal cord.**

**Therefore, the effects of the excitatory transmitters become overwhelming, and the neurons become so excited that they go into rapidly repetitive discharge, resulting in severe tonic muscle spasms.**