Hypnotics And Sedatives

Sleep

- Natural sleep consists of periodic cycles of REM (Rapid eye movement) and NREM (Non – rapid eye movement)
- NREM is very peaceful
- REM sleep is not so restful. 75% of dreams occurs in REM sleep and which are more vivid
- Insomnia is a sleeping disorder characterized by persistent difficulty falling asleep

Hypnotics and Sedatives

- Hypnotics are drugs which produce sleep resembling natural sleep
- Sedatives are drugs that reduces excitement and produces the sleep not resembling natural sleep
- Hypnotics at low doses can act as sedatives
- Sedatives may be divided according to the primary uses into following types

Classification

Hypnotics

Diazepam

- Flurazepam
- Nitrazepam
- Flunitrazepam
- Temazepam
- Triazolam
- Midazolam

Antianxiety agents or sedative

- Diazepam
- Chlordiazepoxide
- Oxazepam
- Lorazepam
- Alprazolam

Classification

Anticonvulsant

- Diazepam
- Clonazepam
- Clobazam

Antipsychotics

- Haloperidol
- Chlorpromazine
- Trifluperidol

Classification of Hypnotics and Sedatives

Barbiturates

- **Long acting**
  Duration of action is for 8 hours or more
  Ex: Barbitone , Phenobarbitone ,
- **Intermediate acting**
  Duration of action is for 4 hours
  Ex: Amylobarbitone, Cyclobarbitone
- **Short acting**
  Duration of action less than 4 hours
  Ex: Hexobarbitone , Secobarbitone
- **Ultra short acting**
  Duration of action less than 1 hour
  Ex: Thiopentone, Methohexitone

Non barbiturates

- **Benzodizepines**

  Ex: Diazepam nitrazepam

- **Alcohols**

  Ex**:** Chloral hydrate

- **Aldehydes**

  Ex: Paraldehyde

- **Miscellaneous**

  Ex: Antihistamines with sedative actions, Hyosine

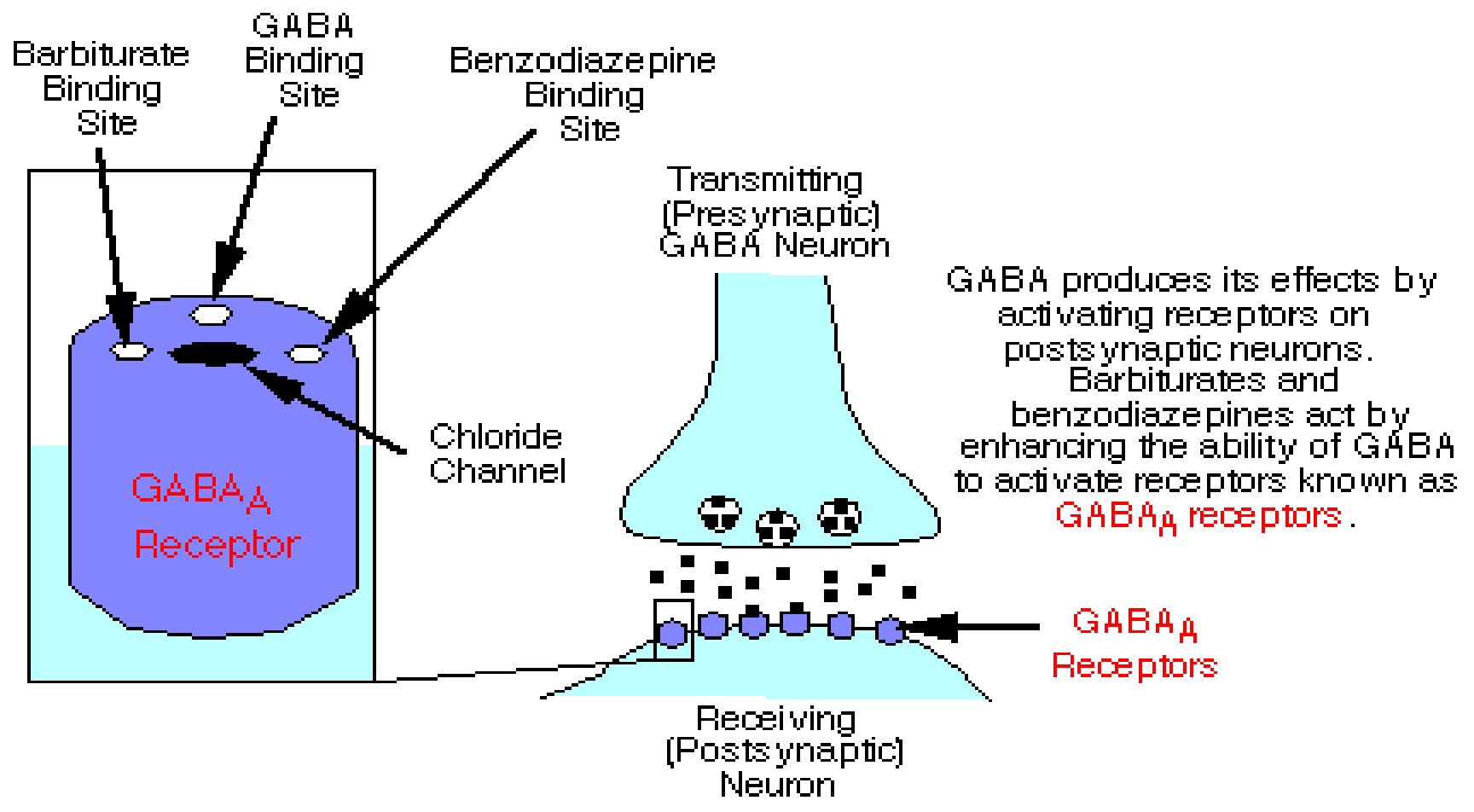
Mechanism of Action

- Hypnotics and sedatives act by producing depression of central nervous system

- They enhance the ability of the inhibitory neurotransmitter, gamma aminobutyric acid (GABA), to activate a type of receptors known as GABA-A receptors.

- These drugs increase the effectiveness of GABA

Mechanism of Action of Hypnotics and Sedatives



Barbiturates

Action on CNS

- Barbiturates are the drugs which reversibly depress the activity of all excitable tissue
- They can achieve various depths of CNS depression from mild sedation to coma
- Barbiturates induce and maintain sleep similar to normal sleep
- They also have anticonvulsant property

Mechanism of Action

- GABA is the principal inhibitory neurotransmitter in the mammalian Central Nervous System (CNS)
- The principal mechanism of action of barbiturates is believed to be their affinity for the GABAA receptor (Acts on GABA
- Like Benzodiazepines, barbiturates potentiate the effect of GABA at this receptor.
- Glutamate is the principal excitatory neurotransmitter in the mammalian CNS.
- Barbiturates also block the AMPA receptor, a subtype of glutamate receptor.

Barbiturates

Respiration

- Respiration is depressed by relatively higher doses.

CVS

- Hypnotic dose of barbiturates produce a slight decrease in BP and heart rate.

Skeletal muscle

- Depress the excitability of neuromuscular junction and reduces the muscle tone.

Renal system

- Barbiturates tend to decrease urine out flow by decreasing BP and increase in ADH release

Barbiturates

Metabolism

- Primarily metabolized in liver by oxidation, dealkylation and conjugation.
- Plasma t1/2 ranges from 12- 40 hrs.

Excretion

- Significantly excreted unchanged in the urine.

Uses

- Except phenobarbitone in epilepsy and thiopentone in anesthesia barbiturates are seldom in use now.
- They are markedly replaced by benzodiazepines

Therapeutic Uses of Hypnotics and Sedatives

- Anti -anxiety agents
- Anti-psychotic agent
- Centrally acting muscle relaxant
- Anticonvulsant (diazepam and clonazepam)
- Pre-anesthetic medication
- Before Electro convulsive theraphy, Cardiac catheterization, Endoscopies

Adverse Effects

- Drug dependence
- It occurs with all sedatives if used for a considerable long time
- Both physiological and psychological dependence may develop
- Drug addiction and abuse

Adverse Effects

- **Side effects**: Hangover ,mental confusion ,dependence impaired performance etc.
- **Idiosyncrasy:** In an occasional patient

  Barbiturates produce excitement. Hypersensitivity

  rashes , swelling of eye lids, lips etc.
- Tolerance and dependence :both cellular and pharmacokinetic tolerance on repeated dose
- Dependence may be psychological or physiological

Contraindication

- Acute intermittent porphyria
- Liver and kidney diseases
- Severe pulmonary insufficiency
- Obstructive sleep apnoea

Drug interactions

- Barbiturates induce the metabolism of many drugs and reduce their efficiency
- Additive action with other CNS depressants

Non Barbiturates

Benzodizepines

- They have high therapeutic index than barbiturates
- They have anticonvulsant , anti anxiety and hypnotic properties.
- They mainly act on limbic system of CNS
- Limbic system is the site of Emotions and Anxiety

Pharmacology of Benzodiazepines

- **Diazepam** produces sedations, reduces aggressiveness causes tranquility of mind
- If increases total sleep time
- If increases the seizure threshold and acts as anticonvulsant
- It has central muscle relaxant action

Therapeutic uses

- In addition to hypnotic and sedative action, they are also used as
- Anti anxiety agents
- Anti-convulsants
- Muscle relaxants
- Pre-anaesthetics agents
- Anaesthesia

Adverse effects

- Light headedness
- Motor in co-ordination
- Ataxia
- Impairment of mental and psychomotor functions
- confusion

Relative side effects

- vertigo , blurred vision , vomiting , epigastric distress etc
- Benzodiazepines are relatively safe drugs

Alcohols

Chloral hydrate

- The principle effect is sedation in small dose
- A slight larger dose results in sleep.

Aldehydes

- **Paraldehyde**: it is a safe hypnotic
- It can be given orally, intramuscularly or rectally
- It also used in control of seizures arising from tetanus, poisons, and Statusepilepticus

Hyoscine

- It is used to prevent motion sickness by its sedative action
- Also used to suppress unwanted secretions during anaesthesia
- It has no analgesic effect

Side effects

- Dry mouth
- Loss of accommodation
- Difficult in micturition