Unit - IV

Peripheral Nervous System

10 × 1 = 10
5 × 2 = 10
2 × 1 = 2
} Must know

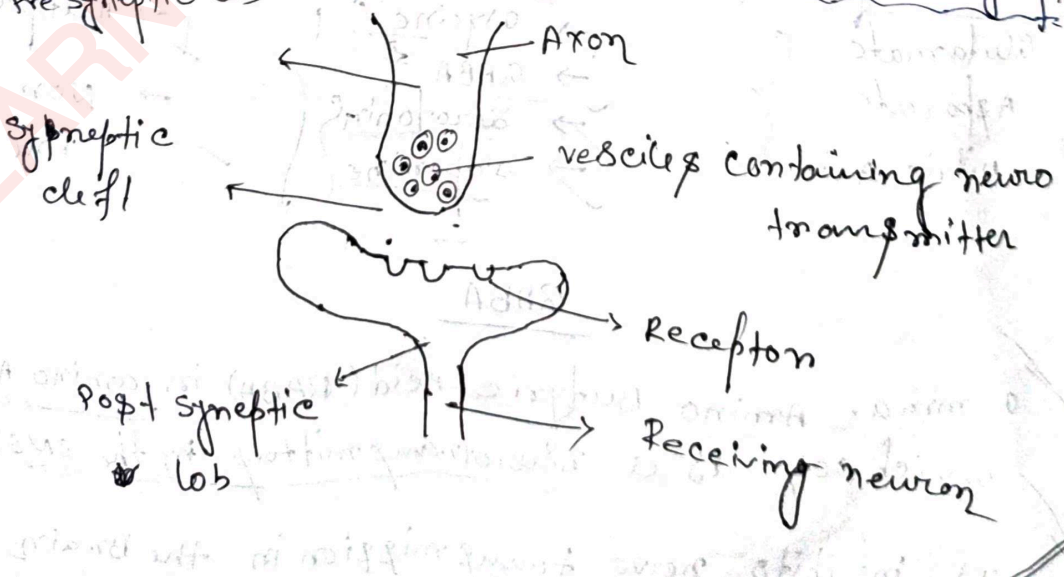
2 × 1 = 2
} Desirable to know

29 Marks

Neurotransmitter & their Mode of Action

- Neurotransmitters are chemical messenger that transmit signals form a neuron to a target cell across a synapse.
- Target cell may be a neuron or some other kind cell like a muscle or gland cell.
- Necessary for rapid communication in synapse.

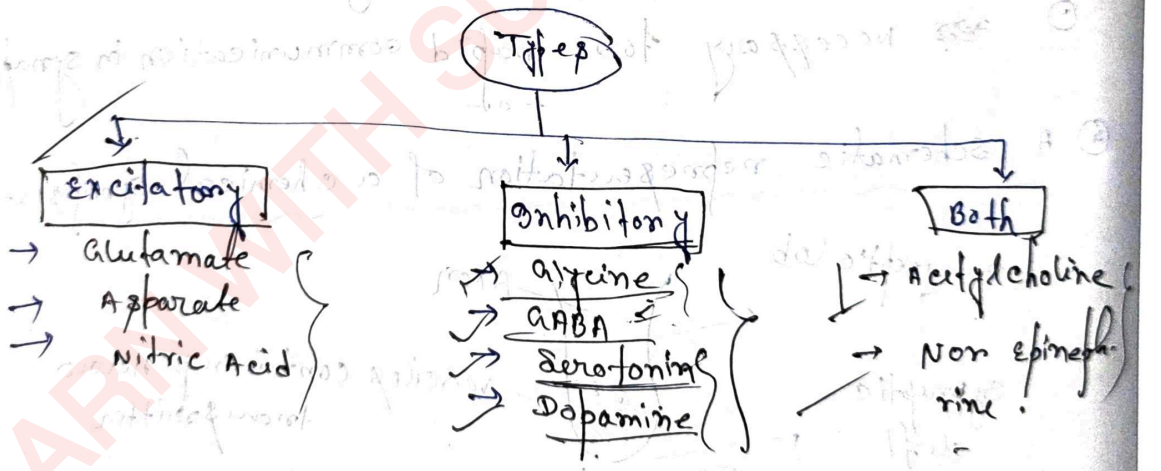
A schematic representation of a chemical synapse:-



Properties of Neurotransmitters

1. Synthesized in the Pre Synaptic lob.
2. Localized to vesicles in the Presynaptic Neuron.
3. Release from the Presynaptic neuron under Physiological condition.
4. Rapidly removed from the synaptic cleft by uptake or degradation.
5. Presence of Receptor on the Post Synaptic Neuron.
6. Binding to the Receptor and give biological response.

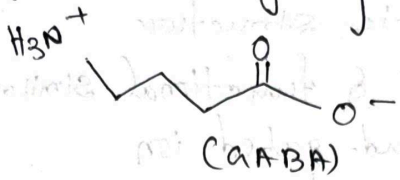
Types of neurotransmitters



GABA

- Gamma- Amino Butyric Acid (GABA) in amino Acid which acts as a neurotransmitter in the CNS.
- It inhibits nerve transmission in the Brain containing nervous activity.
- chemical formula → $C_4H_9NO_2$.

→ GABA is zwitter with deprotonated carboxyl group and Pronoted amino group.



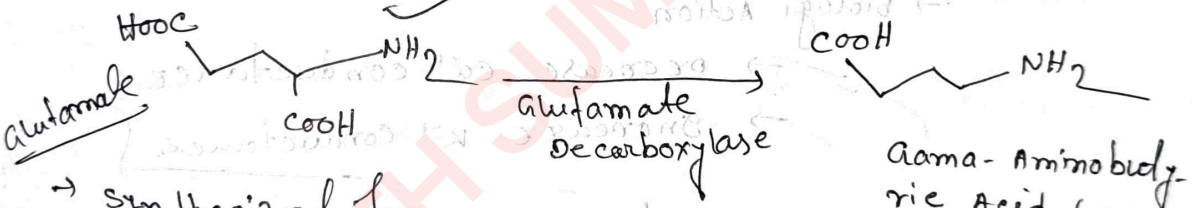
(GABA)

Discovery

→ In 19th centuray → was known as Metabolic of Plant & microorganism.

→ In 1950 Robert & Iranked discoverd thed GABA acts as Inhibitory neurotransmitter in human brain.

Synthesis



Gama-Aminobutyric Acid (GABA)

→ Synthesized form Amino acid - L-glutamate acid in the Presence of GAD.

→ GAD is Present in neurons, Pancreatic cells & in body fluid.

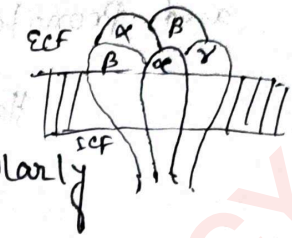
→ GAD Act as a catalyst that removes a carboxyl group form glutamate & Produce GABA.

Classes of GABA Receptor

→ GABA Receptor is of two types -

(a) $GABA_A$ Receptor
(b) $GABA_B$ Receptor.

GABA A Receptor



→ It has Pentameric Structure
→ It has structural & functional similarly with ligand gated ion
→ Each GABA A Receptor contain two alpha two beta & one gama subunit.

GABA B Receptor

→ They are hetero dimers
→ GABA B has been cloned to B_1 & B_2 Receptor.
→ B_1 subunit has GABA binding site whil B_2 subunit interact with G-Protein.
→ biologi Action
→ Decrease Ca^+ conductance
→ Increase K^+ conductance

Function of GABA

→ Relieving Anxiety
→ Releiving Pain
→ Regulating Sex hormones
→ Decrease blood Sugar Level in diabetics

Glutamic acid or glutamate

→ Acidic, non essential amino acid.
→ As a neurotransmitter in CNS.
→ called king of Neurotransmitter.
→ Also called master switch of Brain.
→ Major excitatory of Neurotransmitter.

Synthesis of glutamate

→ Given the excitatory effect of glutamate, it is excluded from the brain by BBB that is blood Brain Barriers is impermeable to glutamate.

→ Thus glutamate in the brain must by synthesied de novo from glucose.

→ TCA → Alpha ketoglutarate → glutamic acid (via transamination)

Receptors of glutamic acid

Ionotropic Receptor

(I) NMDA Receptor (N-Methyl-D-Aspartate)

7 Subunits (GluN1, GluN2A, GluN2B, GluN2C, GluN3A, GluN3B)

(II) AMPA Receptor: (α-Amino-3hydroxy-5-Methyl-4-isoxazole Propionic acid)

4 subunits are present such as
(GluA1, GluA2, GluA3, GluA4)

(iii) Kinate Receptor :-

→ There are 5 subunits are present such as - (~~GluA1, GluA2, GluA3, GluA4~~ GluA5)

GluK1, GluK2, GluK3, GluK4, GluK5

Metabotropic (mGluR)

Group-I	Group-II	Group-III
mGluR1	mGluR2	mGluR4
mGluR5	mGluR3	mGluR6
		mGluR7
		mGluR8

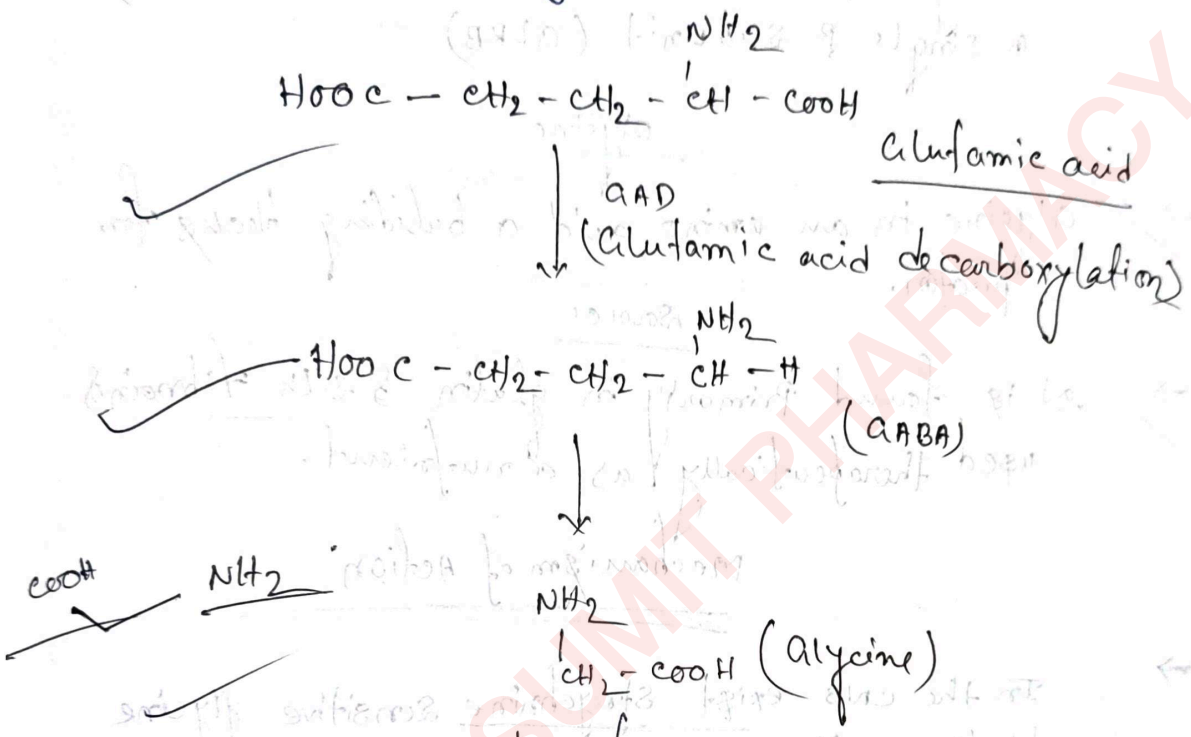
—o—

Glycine

- Glycine is a simplest amino acid which is semiessential amino acid and it should be taken as a nutritional supplement.
- Glycine is also major inhibitory neurotransmitter in the adult vertebrate central nervous system
- glycine receptor (GlyR) is a member of the nicotinic acid Receptor superfamily.

→ It is also known as inhibitory chloride channel protein

Synthesis



Structure

→ Glycine Receptors exists as Pentameric proteins, homo-oligomers of the α isoforms ($\alpha_1, \alpha_2, \alpha_3, \alpha_4, \alpha_5$) or hetero-oligomers which also contain the β-subtype variant which is essential for targeting the Receptor to the Synapse.

① Receptors are arranged as five subunits surrounding a central Pore, with each Subunit composed of four α helical transmembrane Segments.

→ There are Presently four known isoforms of the α subunit (α1-4) of GlyR that are essential to bind ligands ($GLRA_1$, $GLRA_2$, $GLRA_3$, $GLRA_4$) & a single β-subunit (GLRB)

Glycine

→ Glycine in an amino acid a building blocks for protein.

Source

→ It is found Primarily in gelatin & silk fibroins used therapeutically as a nutrient.

Mechanism of Action

→ In the CNS exist Strychnine sensitive glycine binding sites as well as Strychnine insensitive glycine binding sites. The Strychnine-insensitive glycine-binding site is located on the NMDA Receptor complex. The Strychnine-sensitive glycine Receptor complex is comprised of a chloride channel and is member of the ligand-gated ion channel superfamily.

Pharmacokinetic.

→ It is absorbed from small intestine via an active transport mechanism and it is metabolized in liver.

Use

① Glycine is used for treating schizophrenia, stroke, benign prostatic hyperplasia.

② Sometimes it can also be used to treat leg ulcers and heal other wounds by applying on the skin.

D-Tubocurarine

Serotonin

→ Serotonin is a naturally occurring amine synthesized from the tryptophan & commonly found in plants, some fruits, animal tissue & insect venom & It is found in enterochromaffin cells in g.i.T & CNS.

→ This Regulate sleep, body temperature & mood.

→ A hormone melatonine is derived form Serotonin.

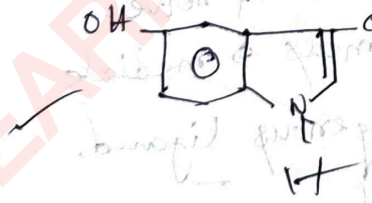
① sleep
② Body temperature

Synthesis

Tryptophan
↓ Hydroxylase
5-Hydroxy Tryptophan
↓ Decarboxylase
5-HT
↓ MAO
5-HIAA (5-Hydroxy Indol Acetic Acid)

MAO → Monoamine oxidase

5-HT → Dehydrogenase → 5-Hydroxy Tryptophol



Pharmacological Action of Serotonin

→ **Action on GIT :-**

① 5-HT act as a local hormone & to regulate Peristelsis movement.

(*) Action on CNS:-

→ It act as neurotransmitter in CNS.

(*) Action on CVS:-

→ 5-HT Produces positive ionotropic effect & chronotropic effect in Myocardium.

(*) Action on Smoothmuscle:-

→ 5-HT constrict the smooth muscles of bronchia & GIT.

(*) Action on Blood vessels:-

→ 5-HT dilate the blood vessels of skeletal muscles, coronary arteries & capilary of skin. ∴ Dialate

(*) Action on platelets:-

→ In enhance the Aggregation of Palfelets & hemostatis..

5-HT Receptors

→ The 5-HT Receptors are the receptors for serotonin They are located on the cell membrane of nerve cells & other cell types in animals & mediate the effects of serotonin as the endogenous ligand.

→ Basically 5-HT are four types-

5-HT_1,

5-HT_2

(*) 5-HT_1 Receptor occour mainly in CNS & some Blood vessels.

→ effect are neural inhibition & vasoconstriction.

$5\text{-}HT_2$

→ This Receptor occour mainly in CNS & many peripheral sites (especially blood vessels, platelets, autonomic Neurons)

$5\text{-}HT_3$

→ This Receptor occora mainly in Peripheral nervous system. effects are excitatory, mediated via direct receptor-coupled ion channel.

$5\text{-}HT_4$

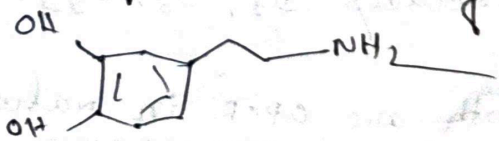
→ This Receptors occour mainly in the enteric nervous system (also in CNS). effects are excitatory causing increased gastrointestinal motality.

Pharmacological Action

- Neurotransmitter
- Hypertension
- Precursor of melatonin
- Nausea & vomiting
- Migraine

Dopamine

→ Dopamine belongs to the family of catecholamines.



→ Hormones, epinephrine & Non-epinephrine are derived form dopamine.

Dopamine synthesis & Metabolism

L-Phenylalanine (amino acid from diet)

↓ Phenylalanine hydroxylase

L-Tyrosine

↓ Tyrosin hydroxylase

COMT, catechol-o-methyl transferase.

L DOPA

↓ DOPA decarboxylase

Dopamine (DA)

↓ MAO, COMT

DOPAC + HVA

Dopamine Receptors

→ Metabotropic G-protein coupled Receptors

D_1-like family

→ Includes Subtype D_1 & D_5

D_2 like family

→ Includes D_2, D_3, D_4.

(Both are GPCR in nature.)

General Anaesthetic

→ General Anaesthetic are those Agents which cause reversible loss of unconciousness this is used before the surgery.

classification of General Anaesthetic

1. Inhaild
   - A. Volatile liquid
     - → Ether
     - → Halothane
     - → Enflurane
     - → Isoflurane
     - → Desflurane
   - B. Gases → Nitrous oxide
2. Intervenus
   - → Theopentone
   - → Benzodiazepene
   - → Ketomine
   - → Propofol
   - → Methoxitone or methoxital.

Stage of Anesthesia

A. Stage of Analgesia
B. Stage of Delirium
C. Stage of Surgical Anaesthesia
D. Stage of Respiratory Paralysis

Stage of Analgesia

→ This is the first stage of Anaesthesia. In this stage the sensation Pain & touch loss.

Stage of Delirium

→ In this stage the conciousness of Body is slowly loss & Patient goes into coma stage.

Stage of surgical Anesthesia

→ In this stage the total body is Anaesthesia patient lost conciousness but their respiration in normal.
→ This is the best stage for surgery.

Stage of Respiratory Paralysis

→ This is the last & most dengerous stage in this stage on longer.
→ Those patient respiratory system can be Paralysis & if patient remain in this stage for long time then Death will occour.

(X) Pre-Anaesthetic medication:-

→ Before surgery or operation the group of medicin which are given with the Anaesthetic is called Pree-Anaesthetic medicine & the process is known as Pre-Anaesthetic Medication.

→ ① Sedation → Barbiturate – (Sleep)
② Analgesia → General
③ Inhibition of Parasympathetic activity → Atropin
④ Antiemtic effect → Promethazine
⑤ Anticogulant → Heparin.

— o —

(x) Classification of General Anaesthetics :–

(A) Inhalational Gas :– → Nitrous oxide → (Night) main inhalation ka Moja lo

(B) Volatile Liquids :–
→ Ether
→ Halothane
→ Isoflurane
→ Desflurane
→ Sevoflurane
Enflurane
→ Hello Ayega Ether Bethe Dagg u ka Seba karo

(#) (2) Brief Notes on drugs of General Anesthetics :–

→ Nitrous oxide :–

⊙ It is colourless, odourless gas
⊙ Heavier than air
⊙ It is non inflammable gas supplied under Pressure in steel cylinders. It is non irritating, But low Potency anaesthetic.

→ A mixture of 70 % N_2O + 25-30 % O_2 + 0.2-2 % another Potent anaesthetic is employed for most surgical Procedures.

Ether (Diethyl ether)

→ Ether is a Potent Anaesthetic, Produce good analgesia & Marked muscle relaxation by Reducing Ach output from motor nerve endings.

→ It is highly soluble in blood.

→ The dose of competitive neuromuscular blockers should be Reduced to about 1/3.

—o—

Sedative & Hypnotics

Pharmalogical Action of Barbiturates:—

(1) Sedation & Hypnotics Action:—

→ When the Barbiturates drug given in Small dose then it shows Sedative action & when it given in Large dose it shows Hypnotics Action.

→ And when barbiturates drugs give regularly for Sedation then it may cause Addiction.

(2) Anaesthetic effect:-

→ Some barbiturates drugs like 'Theopental Sodium' when it given IV form then it cause Anaesthetic effect.

→ And these drugs is generaly given in Pree Anaesthetic medication.

—

(3) Anticonvalsent :-

→ Some category of barbiturates drug is given for the treatment of epilepsy like phenobarbitone, metho-Barbitone.

(4) Effect on Respiration :-

→ Barbiturates drugs basically reduce the hypoxic & chemoreceptor responce & it cause the Respiratory depression.

→ And the Rate of Respiration becomes slow.

→ But when it is given in large dose they cause respiratory paralysis or death.

(5) effect on CVS :-

→ In general dose there are no effect on CVS.

→ But after a long dose it may cause decreage in the heart rate & decreage cardiac output & blood pressure may also be reduce.

(6) Effect on Peripheral Nervous system :→

→ When barbiturates drug is given then it effect the neurohumoral transmission in ganglia of Peripheral nervous System.

→ It Reduce the both the action of sympathetic and Parasympathetic nervous System. basically it blocks the nicotinic Receptor & Reduce cholinergic responce.

(7) effect on kidney :-

→ When barbiturate drug is given it shows effect on kidney it Reduce the Glomerular filtration Rate so the urine output

is Reduce.

(9) Effect on spinal cord :-

→ When barbiturate drug is given it Reduce the Reflex action of spinal cord.

Pharmacokinetics — A D M E

→ It is well absorb orally from stomach & GIT
→ It is available in tablet form.
→ Ad And also available in injection form.
→ Barbiturate are available in two form ionic & non ionic form.
→ ionic form is distributed slowly & unionic form drug can easily distributed and pass into the brain.
→ It Metabolise in to the liver
→ And secreate through urine.

Adverse effect

→ Intolerance
→ Anemia
→ Allergy
→ Addiction

Pharmacological Action of Benzodiazepines

→ Benzodiazepine drug is a sedative & hypnotics category Drugs.

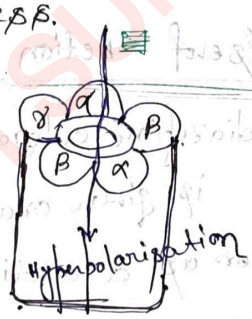
→ Basically benzodiazepines drug bind with GABA Receptor

→ GABA inhibit the Action of Brain or it depress the Brain

→ when Benzodiazepine drugs binds with the GABA Receptor then GABA Receptor contain five Pentamerie form two alpha, two Beta & one gamma.

→ And after binding with the drug Benzodiazepine with GABA Receptor the chloride channel is open and cl- ion goes inside from ECF to ICF.

→ And due to hyperpolaerisation of cl ion the CNS becomes depress.



Pharmacological Action

① Sedative & Hypnotics Action:—

→ Benzodiazepines drugs are used to treatment of Insomnea. It is given for Sedative & Hypnotics Action.

→ when Benzodiazepine drugs are given in small dose then it causes or Sedative Action.

→ And when it is given is large dose it produce Hypnotics Action.

→ And when they are used more than four weeks, then it may produce Addiction effect.

(2)

Reduction of Anxiety & Aggression

→ Basically Benzodiazepine drugs are ~~given in small~~ also use in Anxiety & Reduction Aggression.

→ And it is given before the minery surgery & dental surgery for Reducing the Aggression.

→ It is never be given after four week because it can cause Addiction & tolerance.

(3)

Reduce Muscle tone

→ It is also given in the case of muscle tone.

(4)

Anticonvalsent Action

→ Some drugs are benzodiazepine category like Diazepam & Medazelam which is given orally for the treatment of epilepsy or as a anticonvalsent drug.

(5)

Anteroamensia

→ It is also used in the case of Amensia.

→ This drug delete the old memories & creat new memory.

Pharmacokinetics

→ It is given orally

→ It is well absorbed in stomach and Intestine.

→ They are lipophilic in nature, so they can pass

BBB and effective in the CNS & distributed in the CNS.

→ It is Metabolise in liver in the form of glucoronic Acid & oxidation Reaction.

→ It is Secreate from the urine.

Adverse effect

- → Drowsiness
- → Dizziness
- → Reduce concentration

MOA (Sedative & Hypnotics drugs)

Insomnea + disease

⊛ Sedative & Hypnotics :-

→ Sedative & Hypnotics are those drugs which act on the CNS and they reduce the mental excitement & Mental dipression & Produce the Natural sleep and Sound sleep.

Sedative → Mental excitement
Dipression / Drowsiness

Hypnotics → Relexed
Natural Sleep
Sound Sleep

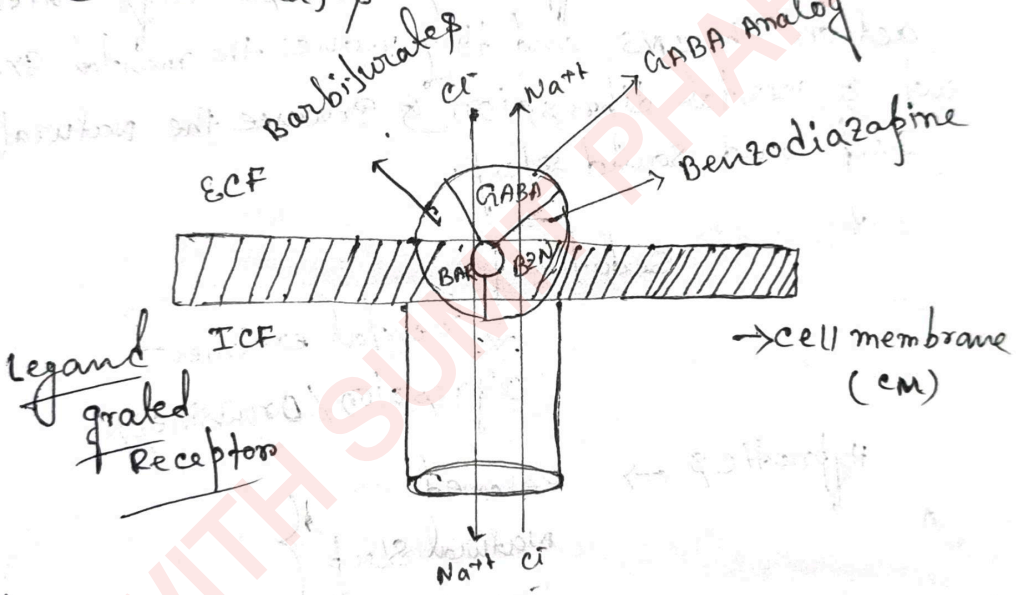
→ Sedative are those drug which don't sleep but they reduce the excitement of Brain & Dipression & Produce Drowsiness. Produce

→ Hypnotics are those drug which have higher concentration than sedative & they basicly relax brain on Complete relax the Brain & Produce natural sleep on Sound sleep.

Mode of Action of Sedative & Hypnotics

→ Basically Sedative & hypnotics drugs are in of 3 category-

1. GABA (Gamma-Aminobutyric Acid) Analog
2. Benzodiazapine
3. Barbiturates



→ When any of the drug (Barbiturate, Benzodizopine, GABA Analog) bind their selective Receptor. like Benzodizopine bind with Benzodizopine Receptors, Barbiturate bind with the Barbiturate Receptor & these drug bind with the Receptor then channels are open and chloride ions moves then channel Receptor becomes high polorized the transmision of Na^+ is completely stoped in that case brain becomes relax and the excitement of Brain is Reduced & Sedative & hypnotics action Produce in our CNS.

Classification of Sedative & Hynotics Drugs :-

Barbiturates :-

- Long Acting → Phenobarbitone
- Short Acting → Buto barbitone
- Ultra-short Acting → Thiopentone, Methohexitone

Trick

→ Agar Barbi ko Sule hai to Fan butaw Thapki do Mathe P Aur Mast tone Mau lori gaw

Benzodiazepines - Hypnotics

→
- Diazepam
- Flurazepam
- Nitrazepam
- Triazolam
- Temazepam
- Alprazolam

Trick

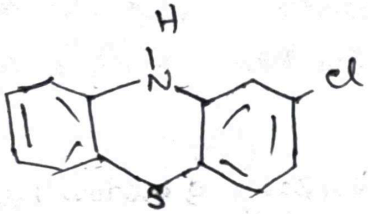
→ Diya ko flu ho geya tha night main Par Tripathi ko tameez nehi Rat var Benzo Par Alaf ga tha Raha.

Newer Non benzodiazepine :-

- Zolpidem
- Zaleplon
- Zopiclone

Trick

→ Nayea log Jal Bichate hai Pind main Plan ke Sath clone Banate hai.



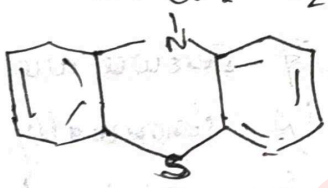
2-chlorophenothiazine

+ Cl-CH_2-CH_2-CH_2-N(CH_3)(CH_3) · HCl

3-chloropyl diethylamine Hydro chloride

Reflux

Toluene Sodamine



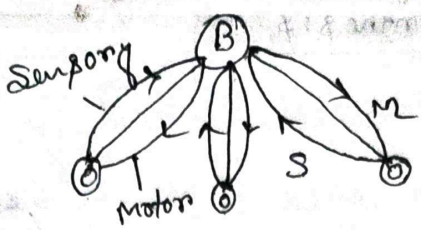
· HCl

Chlorpromazine hydrochloride

— o —

Anticonvulsant – Epilepsy / Seizure

1) Most commonly Seizure is also known as Epilepsy.
2) It is derived form Greek word, Epilamber which means To Sieze.
3) It is an neurological disorder, in which the neurohormonal transmission of the brain is ~~commonly~~ completely effected.



→ In epilepsy there is a abnormal sensory & motor neuronal discharge so function of an organ in body or function of muscles is completely changed and seizures are convulsions are comes out which is called convulsant / epilepsy.

→ Seizure Paroxysmal events due to abnormal excessive neuronal activity in the Brain cortex.

→ The clinical characteristics of seizure are result of the area of brain that is abnormally stimulated.

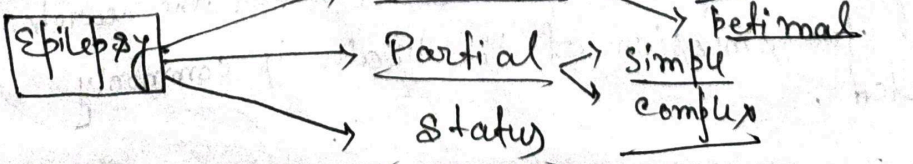
→ 5-10%. of the Population will have at least on seizure in their lifetime.

→ Highest incidence is in childhood and late adulthood.

Symptoms

- chronic Recurrent Proximal changes
- Loss of consciousness.
- Abnormal sensation
- duration sec - minute.

classification of epilepsy



① Generalized

Entire Brain envolve in Seizures, it is not arrived form any single Part of the It is of 2 types-

Grandmal / Tonic clonic seizure:-

→ It is also called tonic clonic Seizure.

→ In the Seizure begning is strad form oera, then after bilateral muscular jurk.

→ In this Seizure the loss of consciousness completely envolve and muscle spasm.

→ It remain for 2-5 minutes.

Petimal (Absence Seizure)

✓ It is also called absence Seizure. It is basically appear in children.

✓ In this Seizure also the completely loss of consciousness & loss of ~~seen~~ speech generally seen.

✓ It remain for 1-30 second.

② Partial / Focal

This type of Seizure is generally seen any Part of Brain basically temporal lobes.

It not cover in full brain, and its symptoms start begning from local body organ.

D It is of two types-

(A) Simple :-

→ This is also called jacksonin motor epilepsy.

- It is basically contain Part of brain complex,
- Some muscle, thumb, toe.
- Don't loss of conciousness and time duration 1-2 minute.

(B) complex :-

→ It is also called Psychomotor.

→ uncommon (Patient found in rare case)

→ Extensive, swalling, cheving.

→ Time duration 1-2 minutes.

(3) Status :-

→ In this type of sizure, the brain damage of Patient.

→ The time duration of Seizure 30 min.

—o—

Classification of Anticonvulsant drugs

1. Barbiturate → Phenobarbitone
2. Deoxy barbiturate → Primidone
3. Hydantoin → Phenytoin, Fosphentoin
4. Iminostibene → carbamazepine, Oxcarbazepine
5. Succinimide → Ethosuximide.

6) Aliphatic carboxylic → valporic Acid, Sodium valporate, Divalporex.

7) Benzodiazepines → clonazepam, Diazepam, Lonazepam, clobatam.

8) Phenyltriazine → Lamotrigine.

9) Cyclic GABA → GABApentin, Pregabalin.

10) Newer drugs → Topiramate, Zonisamide, Laco Samide, vigabatrin, Ticagabine, Levetinacetam.

Trick

Hai Babar dev ali inme Success Pa na ho to Bau Jaw Sannasi in neye chorkore Main Na Pade.

MODE OF ACTION

3 group

- Facileate GABA → Barbiturate, Deoxy Barbiturate, Benzodiazepines
- Block neuronal ion channel → Hydantoin (Cl^- open), Succinimide (Ca^{++} closed)
- unknown → valproate.

Short note :-

~~Valporic~~
Valproic Acid

→ MOA :-

⊙ Exact Mechanism unknown. Possible Mechanism Proposed.

① It Inhibitis Metabolism of GABA via down regulation of GAT-1 & GABA-3 transport Proteins & depressed CNS.

② Some time it blocks (T type) calcium currents.

clinical indications :- (Broad-spectrum AED)

→ Absence Seizure, tonic-clonic Seizure, myoclonic Seizure, Partial Seizure.

Pharmacokinetics :-

① It is absorbed by orally.
② 70-90% Protein bounding
③ Metabolized to glucoronide conjugate into the liver.

$T_{1/2}$ = 15 hr.

Advarse effect :→

→ Nausea, vomiting
→ Hepatoxicity.
→ It Produce teratogenecity, during Pregnancy into new born baby.

Phenytoin

→ Limits the development of spontaneous seizure activity & Reduced the spread of the seizure.

→ MOA

Basically Phenytoin drugs blocks the voltage-gated Sodium channel & stop the transfer of Na^+ ion & the Muscle conn-transaction is stop.

clinical indication (Broad-spectrum AED)

→ used for generalized tonic/clonic seizure, Partial Seizure, status epilepticus.

Pharmacokinetics

- It is taken from orally.
- Phenytoin is highly fat soluble.
- Readily absorbed from the GI tract.
- It is metabolized in the liver by the help of enzyme CYP2C9/10.
- The elimination of phenytoin follows zero-order kinetics.
- $T_{1/2}$ = 24 hr.
- The excretion rate is slow because it lipophilic in nature & Protein bounding.

A D M E

Adverse effect

→ Skin rash
→ mental confusion
→ Dizziness

contraindications:- Sinus bradycardia And SA Block.

Alcohol & Disulfiram

Ethyl Alcohol (Ethanol)

→ Alcohols are hydroxy derivative of Aliphatic hydrocarbons.

→ Alcohols is manufacture by fermention of sugers.

→ Fermentation Proceeds till alcohol content reached 15%.

→ Starch —Convertase→ Maltose.
→ which can be fermented by yeast to Produce
Alcohol.

MOA

→ Alcohol has been shown to enhance GABA ~~Release~~ Release of $GABA_A$ sites in the Brain.

→ It also inhibits NMDA receptors.

→ Action of 5-HTon 5-HT inhibitory autoreceptor

→ It Also blocks Na^+ channel.

Phcarmacological Action

① Local Actions:-

→ Ethanol is a mild ~~co~~ rube facient & conferring taut when rubbed on the skin. By evaporation it Produce cooling.

→ Applied on delicate skin or mucous membrane if produce irritation & burning sensation
→ concentrated alcohol should not be applied in the mouth, nose.

(2) CNS

→ Alcohol is neuronal depressant.
→ These are primarily inhibitory - apparent excitation & euphoria is experienced at lower plasma concentration.
→ Mood & feelings are altered.
→ Alcohol can produce anaesthesia.

(3) CVS

Small dose :- Produce only cutaneous & gastric vasodilation
→ skin is warm & BP is not affected.

Moderate dose :- when it gives moderate dose it increase BP.

Large dose :- cause direct myocardial as well as vasomotor center & there BP is fall.

(4) * Blood

→ Regular intake of small to moderate amounts of alcohol has been found to raise HDL cholesterol levels & decrease LDL oxidation.
→ mild Anaemia is common in chronic alcoholics.

(5) Body temperature

→ Alcohol is reputed to combat cold.
→ High dose depress temperature regulating center.

(6) Respiration

→ In small dose it don't produce any effect but in large dose it produce respiratory depressant.

(7) GIT

→ Dilute alcohol put in the stomach by Ryl's tube is a strong stimulant of gastric secretion.
→ Higher concentration inhibit gastric secretion cause vomating, mucosal congestion

(8) kidney

→ Diuresis is often noticed after alcohol intake.
→ This is due to water ingested along with drinks as well as alcohol induced inhibition of ADH secretion.

Pharmacokinetics ADME

→ Absorption from intestines is very fast.
→ Peak levels are attained after - 30 min.
→ Absorption of alcohol from skin of Adults

is minimal but may be significant in infants.

→ Alcohol gets distributed widely in the body.

→ Alcohol is oxidized in liver to the extent of 98%.

Ethyl Alcohol —(Alcohol dehydrogenase)→ Acetaldehyde —(Aldehyde dehydrogenase)→ Acetate + CO_2 + H_2O

→ Excretion of alcohol occurs through kidney and lungs.

Contraindications

→ Intake of alcohol should be avoided by

1. Peptic ulcer
2. Hyperacidity
3. gastroesophagal reflux patients.

Disulfiram

→ Disulfiram is an aldehyde dehydrogenase inhibitor. It Probibits the activity of aldehyde dehydrogenase & enzyme found in the liver.

→ In the united states disulfiram is sold under brand name "Antabuse"