Qn paper III.
CNS Pharmacology

ANTICONVULSANTS & NEURO TRANSMITTERS.

I.Name the following

1.Agent which mediate sensation of Noxious stimuli in the dorsal horn of Spinal cord. (Substance –P)
2.Breeds of cattle in which Idiopathic epilepsy is seen as an inherited condition. (Brown swiss.)
3.Important non peptide transmitters of CNS. (Acetyl choline, Nor. Adrenaline, Adrenaline, Dopamine , Histamine, 5 HT, GABA.)
4.Three pituitary peptide acts as neurotransmitters. (Prolactin, Beta Endorphins, Oxytocin.)
5.Three families of Opioid peptides.(Endorphins, Enkephalins and Dynorphins.)
6.Three monoamines acting as neurotransmitters. (Norepinephrine, Dopamine, 5-HT.)
7.The anticonvulsant recommended for controlling convulsive disorders associated with infectious neuropathies such as viral encephalitis and distemper.(Primidone.)
8.Two excitatory amino acid neuro transmitters. (Glutamate and Aspartate)
9.Two inhibitory amino acid neurotransmitters. (GABA, Glycine)
10.Two main excitatory amino acid receptor subtypes .(NMDA, AMPA.)
11.Two Important neuropeptide transmitters of CNS . (Endorphins, Substance-P,
12.Two hormones acting as neurotransmitters.(Vasopressin, Oxytocin.)
13.Two Tachykinin Transmitters of CNS. (Neurokinin-A, Neurokinin B, Substance-P) Angiotensin-II.)
14.Two sulfonamide derivatives with anticonvulsant action.(Acetazolamide, Sulthiame, Zonisamide)

II.State true or false.

1.Acetyl choline is having both excitatory and inhibitory action.(T)
2.Angiotensin -II is a peptide neuro transmitter. (T)
3.As a neuro transmitter prostaglandins are excitatory and inhibitory in nature.(T)
4.As a neurotransmitter L-Glutamic acid is excitatory in nature.(T)
5.Acetylcholine is having both inhibitory and excitatory CNS effect.(T)
6.Among Muscarinic receptors M1 is most abundant in brain.(T)
7.Alpha and **β** receptors of Nor adrenaline are G- protein coupled .(T)
8.Accumulation of c AMP is the mechanism of excitatory **β** -adrenoceptor in CNS.(F)
9.All the 5HT receptor subtypes except 5HT-3 are G protein coupled.(T)
10.Amino acids like Glutamate and Aspartate are neurotransmitters having excitatory effect.(T)
11.Amino acids like GABA , Glycine and B-Alanine are neurotransmitters having inhibitory effect.(T)
12.ATP acts as a transmitter in the CNS and autonomic ganglia .(T)
13.As a transmitter Glycine is mainly seen in spinal cord and have inhibitory action.(T)
14.Acetyl choline is having both excitatory and inhibitory central effect.(T.)
15.As a neurotransmitter Glycine is seen only in spinal cord.(F)
16.As an antiepileptic agent 1-2 mg/kg of phenobarbitone can be given orally in dogs.(T)

17.A large concentration of GABA is seen in retina. (T)
18.Beta endorphins are derived from Pro-opiomelanocortin.(T)
19.Beta endorphin is an endogenous opioid compound.(T)
20.Bradykinin and Cholecystokinin are peptide transmitters.(T)
21.Carbamazepins can be used as an anticonvulsant in dogs.(T)
22.Carnosine and Calcitonin are peptide transmitters.(T)
23.Dopamine is mainly seen in Basal ganglia and Limbic system(T)
24.Dopamine is predominantly excitatory in nature.(F)
25.Diazepam is contraindicated in Greyhounds breeds of dogs.(T)
26.Diazepam and Barbiturate produce Antagonistic effect on GABA receptors.(F)
27.Dopamine is mainly inhibitory in action.(T)
28.Diazepam is not used orally as a maintenance anticonvulsant in dogs because of its shorter half life.(T)
29.Dopamine releasing neurons lack the enzyme dopamine beta hydroxylase.(T)
30.Dopamine is predominantly inhibitory in action.(T)
31.Defficiency of dopamine causes extrapyramidal disturbances.(T)
32.Dopamine is linked to fine control movement and disturbance of behavior.(T)
33.D_1 receptors are located pre synaptically and act via Adenyl cyclase.(F)
34.D_2 receptors are pre and post synaptical and not act via c AMP.(T)
35.D_5 is coupled to G proteins and stimulate Adenyl cyclase.(T)
36.D_3 and D_4 are coupled to G protein and suppress adenyl cyclase.(T)
37.D_3 receptors are having post synaptic inhibitory action.(F)
38.D_2 receptors have no action on cAMP. (T)
39.Ethosuximide selectively inhibit transient type calcium channel.(T)
40.Ethosuximide can not be recommended in pregnant animals.(T)
41.Epinephrine neurons are found in Reticular formation. (T)
42.Epinephrine containing neurons are found in the Reticular formation.(T)
43.Felbamate inhibits NMDA evoked response.(T)
44.Felbamate inhibits GABA inducing response.(F)
45.Greater concentration of GABA is seen in Basal ganglia, Hypocampus, Cerebellum and hypothalamus in the brain.(T)
46.$GABA_A$, is more prevalent than other subtypes.(T)
47.$GABA_A$ is a ligand gated chloride ion channel.(T)
48.$GABA_B$ act via G protein and stimulate conductance of Chloride channels.(T)
49.Glycine is seen in retina.(T)
50.Glycine is an inhibitory neurotransmitter.(T)
51.Glycine stimulate chloride conductance.(T)
52.Glutamate and Aspartate are excitatory in brain(T)
53.Glutamate and Aspartate are G protein coupled receptors.(T)
54.Higher concentration of 5 HT is seen in blood platelets and G.I. Tract.(T.)
55. 5 -HT inhibits the pain pathways in spinal cord.(T)
56.Histamine is mainly having inhibitory action on neurons (T)
57.Histamine receptors are mostly seen in posterior hypothalamus.(T)
58.Histaminergic neurons have a well developed reuptake process mechanism.(F)
59.Higher concentrations of Serotonin is seen in Blood platelets and G.I. Tract. (T)
60. 5-HT is having both excitatory and inhibitory effect.(T).

61.In the Brain histaminergic receptors are mostly seen in posterior hypothalamus(T)
62.In the CNS and peripheeral nervous system the mechanism of transmission of nor Epinephrine is the same.(F)
64.Inhibition of prolactin secretion is mediated by D_2 receptors.(T)
65.In Brain nor adrenaline is seen mainly in Hypothalamus, Limbic system and Reticular formation .(T)
66.In cats the $t_{1/2}$ of primidone is short .(F)
67.In cats potassium bromide is not recommended as it produce severe asthma .(T)
68.Kinate receptors, NMDA receptors and AMPA receptors are ion gated receptors.(T)
69.L-glutamic acid is excitatory in action.(T)
70.Largest concentration of GABA is seen in retina.(T.)
71.Large concentration of Dopamine is seen in Basal ganglia and Limbic system.(T.)
72.Locus cerulus and Reticular formation are involved in the mechanism of sleep, mood, wakefulness, emotion behavior , temperature etc.(T)
73.Muscarinic receptors are non G protein coupled receptors .(F)
74.More than 40 different neurotransmitters have been identified in the CNS.(T)
75.Neuropeptide transmitters are synthesized instantly at the time of use and are diffused in to the tissues.(F)
76.Neuropeptide neurotransmitters are having short duration of action .(F)
77.Nor epinephrine is seen in Locus cerulus and Reticular formation.(T)
78.Neuro peptide neurotransmitters are less potent than non peptides .(F)
79.Nicotinic receptors are examples for iono receptors.(T)
80.Nitric oxide is a diffusible mediator.(T)
81.Neuropeptide transmitters are less potent than others (F)
82.Nitric oxide mostly occurs in regions of the brain that are responsible for long term behavior and memory.(T)
83.Nitric oxide is stored in vesicles.(F)
84.Nitric oxide is synthesized only at the time of use .(T)
85.NMDA receptors permits the passage of Calcium ions.(T)
86.Nor adrenaline is having both excitatory and inhibitory action on CNS.(T)
87.Nitrous oxide is a convulsive anaesthetic. (T)
88.Primarily Substance -P is excitatory in nature.(T).
89.Pro-enkephalins and Pro- dynorphins are long acting neurotransmitters.(F)
90.Pro-opiomelanocortin is a long acting neurotransmitter.(T.)
91.Prostaglandins and thromboxanes are diffusible mediators in CNS.(T)
92.Primidone is not recommended in cats as it is neurotoxic.(T)
93.Primidone is mostly recommended in dogs.(T)
94.Phenobarbitone , primidone and phenytoin can increase serum alkaline phosphatase Level.(T)
95.Primidone is not advisable in cats as its $t_{½}$ is very long .(T).
96.Release of all transmitters in the CNS are voltage dependent .(T)
97.Release of transmitters in the CNS require the influx of calcium ions in to presynaptic terminals .(T)
98.Reticular formation is important in the control of sleep and wakefulness.(T)
99.Several types of muscarinic receptors M1 to M5 occurs in the CNS .(T)
100.Serotonin inhibits pain pathway in spinal cord.(T)

101.Substance-P mediate sensation of noxious stimuli in the dorsal horn of spinal cord.(T)
102.Sodium chloride is the drug of choice in acute bromide toxicity.(T)
103.Sulphonamides and salicylates increase the CNS depressive response.(T)
104.Substance –P is mainly seen in root of spinal cord, Hypothalamus.(T)
105.Substance- P is present in Brain and Intestine.(T)
106.Sleep and Wakefulness are regulated by 5 HT.(T)
107.Serotonin inhibits pain pathway in Spinal cord. (T)
108.The Ketamine sensitive NMDA receptors are Glutamate gated cation channels.(T)
109.The following are examples for neuropeptide neurotransmitters of CNS- **β** endorphins,. Enkephalins, Substance-P, Vasopressin, Oxytocin, Somatostatin, Angiotensin II, Cholecystokinin, Neurotensin.(T)
110.Thyrotropic releasing hormone is from hypothalamus and is a neurotransmitter .(T)
111.The major side effects of phenobarbitone is polyphagia, polydipsia and Wt. gain.(T)
112.The effect of Diazepam is decreased by Rifampicin.(T)
113.The effect of Diazepam is prolonged with Cimetidine.(T)
114.The antiepileptic drugs exert their action mainly by GABA stimulation and inhibition of Sodium and Calcium channels.(T)
115.The release of Neuropeptide transmitters are not depended on Calcium. (F)
116.Tachykinins includes peptides like- Substance-P, Neurokinin A and neurokinin B.(T)
117.Vomition is mediated by D_2 receptors.(T)
118.Zonisamide acts by inhibiting voltage dependent Na^+ and K^+ channels.(T)
119.Zopiclone is a hypnotic and is an agonist of GABA receptors.(T)

III.Fill up the Blanks with appropriate answers given at the bottom of this question.

1.AMPA receptors permit ..... influx and .....efflux (Sodium, Potassium.)
2.Among dopaminergic receptors .....subtype stimulate Adenyl cyclase and .....subtype suppress adenyl cyclase (D_5, D_3 and D_4)
3.Among Muscarinic receptors.....subtype is most abundant in Brain.(M1)
4.Among barbiturates Phenobarbitone,.....and Metharbital are the common drugs used against epilepsy. (Mephobarbital)
5.Beta endorphins mediate .....(Analgesia.)
6.Cluster epilepsy is commonly noticed in .....and.....breeds of Dogs (German shepherds, Golden retrievers.)
7.Dopamine deficiency in nigrostriatal pathway is associated with ……..in human beings (Parkinsons disease.)
8.D_1 (Dopaminergic) receptors are located.....synaptically and act via Adenyl cyclase cAMP (Post)
9.Excess dopamine activity has been implicated in …….. (Schizophrenia.)
10.Fine control movement is mediated by .....receptors. (Dopamine

11.$GABA_A$ receptors act via ligand gated .....ion channels (Chloride)
12.$GABA_B$ receptors act via G protein and stimulate the conduction of .....channels (Potassium.)
13.GABA is an ……neurotransmitter (Inhibitory)

14.Glycine is an ……. Neurotransmitter (Inhibitory)
15.Glycine is mainly seen in .....(Spinal cord.)
16.H_2 receptors acts through ……generation.(Adenyl cyclase and cAMP.)
17.Histamine receptors are mainly .....in action (Inhibitory)
18.Hyperplasia of the gum is one of the side effects seen in chronic users of .....as anti convulsants (Diphenyl hydantoin.)
19.Inhibitory neurotransmitter GABA is seen mainly in .....and Glycine in..... ..... . (CNS, Spinal cord)
20.In CNS largest concentration of Dopamine is seen in .....and.....(Basal ganglia and Limbic system.)
21.In Brain Substance-P is having excitatory action on ..... neurons.(Dopaminergic)
22.In the dorsal horn of spinal cord Substance-P mediate the sensation of .....(Pain.)
23.If convulsions are confined to a single limb or group of muscles it is called '.....".epilepsy.(Jacksonian.)
24.In Hardpad disease the anticonvulsant of choice is .....(Primidone.)
25.Kapa 1 receptors produce .....analgesia.(Spinal .)
26.Kinate receptors are permitting Sodium influx while N-methyl D- Aspartate (NMDA) receptors are permitting passage of .....(Calcium.)
27.M_1 (muscarinic)receptors are most abundant in .....coupled to ..... proteins (Brain, G proteins.)
28.Mephobarbitone is available as .....(Mebaral.)
29.Nitric oxide is synthesized and released …….....of use and act as a Mediator (at the time)
30.N-Methyl Phenobarbitone is otherwise called as .....(Mephobarbitone.)
31.Phenytoin , Carbamazepins , Sodium valproate and Lamotregen acts as anticonvulsant by their .....channel blocking action.(Sodium)
32.The anticonvulsant action of Ethosuximide is due to blockage of .....channels. (T type calcium.)
33.The active ingredient of Calmpose is.....(Diazepam.)
34.The active ingredient of Valium is.....(Diazepam)
35.The most important Amino acid neurotransmitters in CNS are ....., ..., ... and .....(GABA, Glycine. Aspartate, Glutamate)
36.. . .....sub type of Dopamine receptors are coupled to G proteins and supress Adenyl cyclase. (D3 and D4)
37. Vigabatrin , Tiagabine and Gabapentin exert their anticonvulsant effect by activating ..... receptors.(GABA.)

Answers: (CNS, Spinal cord, Spinal analgesia , Post, Inhibitory, Excitatory, GABA, Glycine, Adenyl cyclase, CAMP, T type Calcium, Chloride, Basal ganglia, Limbic system, Parkinsons disease, Diazepam, Grey hounds, Myasthenia gravis, Diphenyl hydantoin, D5, D3 and D4, Schizophrenia, Narcosis, Glutamate , Dopamine, Aspartate. At the time of use, M1, Jacksonian, Mephobarbitone, Meberal, Release always, Dopaminergic, Pain, Analgesia, German shepherds, Sodium, Potassium, Golden retrievers, Primidone, Brain, G-protein)

IV. Explain in 1-2 sentences.

1.Anti convulsant action of Barbiturates--Binds to GABA and increase chloride conductance, Inhibits Calcium dependent release of neurotransmitters, depress glutamate induced neuronal depolarization through AMPA receptors, Also depress Sodium and Potassium channels.

2.Epilepsy-- refers to a disorder of brain function characterized by the periodic and unpredictable occurrence of seizures.

3.Grandmal--characterised by tonic rigidity of extremities followed by massive clonic jerking for several minutes.

4.Petitmal-- characterized by momentary loss of consciousness associated with staring and cessation of activity, There is clonic jerking of eyelids but no motor activity.

5.Idiopathic epilepsy--recurrent seizures resulting from a functional disorder of the brain. No specific cause is identified.

6.Cluster epilepsy-- are multiple isolated seizures in a short period , 3-15 seizures in succession over 24-48 hrs.

7.Status epilepticus-- epileptic seizures that are so frequent and so prolonged,, before recovering from the initial seizure there is subsequent generalized seizure. There may be exhaustion and death.

8.Treatment of phenobarbitone overdose-- Activated charcoal, Alkalinisation of urine, peritoneal dialysis, antidotes.

V.Underline the correct answers from the given ones.

1. Felbamate is an anticonvulsant drug and it acts by a) Blockade of NMDA receptor-mediated neuronal excitation b)Inhibition of voltage depended Na and Ca channels c)Potentiate GABA mediated neuronal inhibition d) All the above.

2. Release of transmitters in the CNS require a) The influx of calcium ions in to presynaptic terminals b)The influx of calcium ions in to postsynaptic terminals c) None of the above d) Both 1 and 2 above.

3. Following are neuropeptide transmitters of CNS a) Endorphins b) Substance-P c) Angiotensin-II. d) All the above.

4. One of the following is a pituitary peptide acts as neurotransmitters a)Prolactin, b) GABA c) Glycine d) Angiotensin-II.

5. An excitatory amino acid neuro transmitter a)Glutamate b) GABA c) Glycine d) None of the above.

6. An inhibitory amino acid neurotransmitter a) Aspartate b) Glycine c) Glutamate d) None of the above.

7. A hormonal neurotransmitter a) Vasopressin b) Glutamate c)GABA d)Aspartate

8. Cattle breed in which Idiopathic epilepsy is seen as an inherited condition a) Jersey b) Vechur c) Swiss brown d) None of the above

9. Glycine as a transmitter mainly seen in a) Spinal cord b) Medulla c) Cortex d) Hypothalamus

10. D1 receptors are a) located post synaptically and act via Adenyl cyclase cAMP b) located pre synaptically and act via Adenyl cyclase c AMP. c) located pre and post synapticaly and act via Adenyl cyclase cAMP d) Not act via Adenyl cyclase c AMP.

11. Glycine is an inhibitory neurotransmitter seen in a) Retina b) Spinal cord c) lower brain stem d) all the above.

12.On Dopaminergic neurons Substance P is having a) an excitatory action b) an inhibitory action c) no action d) action differs on different sites.

VI.**SHORT NOTES**

1. **Classify** neurotransmitters of CNS with examples?---

A. Small molecule rapidly acting transmitters.

a)Acetyl choline- act as excitatory and inhibitory

b)Monoamines:1) Nor epinephrineand Epinephrine-Excitatory and inhibitory.
2) Dopamine- Inhibitory
3) 5-Hydroxyt tryptamine- Inhibitory.

c)Amino acids: 1) Gama amino butyric acid –Inhibitory.
2)Glycine- Inhibitory.
3) Aspartate and Glutamate- Excitatory.

B. Slowly acting neuropeptide transmitters. Enkephalins, Beta endorphins, Vasopressin, Oxytocin, Growth hormones, Substance-P, Cholecystokinin, Angiotensin II, Neurotensin

2.Neuromodulators---It originate from a cellular non synaptic site-influence the excitability of nerve cells differently from neurotransmitters.Eg. Carbondioxide, Ammonia originate from neurons or glia cells-modulate the activity through non synaptic –circulating steroid hormones, locally releasing adenosine and prostaglandins .

3.Phenytoin sodium. ---Hyadantoin derivative, not useful for emergency treatment, undesirable pharmacokinetic profile in animals. Stabilizing effect on neuronal membranes, depresses the motor areas of brain. Chronic use leads to hepatic hypertrophy and necrosis, polyphagia, inhibit ADH secretion, induce hepatic enzymes-enhance metabolism of many drugs. Dogs- 10-35 mg/kg TID.

4.Clonazepam.--- More potent benzodiazepine than diazepam- enhance effect of GABA both in brain and spinal cord- decrease seizer spread- blocks spinal reflexes- 100% bioavailability. Contra indicated in hepatic disease and hepatic enzyme inducers like Rifampicin- used for short term control- Dogs-0.05 -0.2 mg/kg i/v.

5.Diazepam.--- Strong anticonvulsant - crosses BBB faster than any other anticonvulsant-metabolized to nordiazepam and oxazepam with 1/3 activity- tolerance in 1-2 weeks so not good for long term use- drug of choice in status epilepticus. Dogs and Cats0.5 mg/kg, i/v. repeat 1-2 times in first 2 hrs. Horse 25-100 mg total, i/v. in dextrose.

6.Signal Transduction in CNS.--- Neurotransmitters (first messenger) link to receptors of post synaptic membranes- conformational changes occur in receptor protein-enable it to interact with a second element in the system the G protein-this in turn transduce the signals to an amplifying enzyme (a third component), This activate the "Second messenger"which interact with various cellular process to involve the ultimate action. Eg: for second messengers , Adenyl cyclase, c AMP, Guanyl cyclase, Phospholipid hydrolysis etc.

7.False neuro transmitters. ---Agents which are incorporated in the synthetic pathways of neurotransmitters and occupy the positions of neurotransmitters and produce only reduced response. Eg.Alpha methyl dopa , like dopa it is successively decarboxylated and hydroxylated in its side chain to form false neurotransmitter (Alpha methyl norepinephrine).This compound is less potent than nor epinephrine -replace the later in adrenergic nerve terminals-its release by nerve impulse produce considerably reduced response.

8.Classify antiepileptic drugs with examples.---

a. Barbiturates---- Phenobarbitone.
b. Deoxy barbiturates-----Primidone.
c. Hydantoin----- Phenytoin
d. Benzodiazepins-----Clonazepam.
e. Bromides-----Bromides of Sodium ,Potassium, and Ammonium.
f. Aliphatic carboxylic acid----Valproic acid.
g. Succimides----Ethosuximide.
h. Iminostilbene---- Carbamazepins.
i. Phenyl triazine---- Lamotrigin.
j. Cyclic GABA analog----Gabapentin.
k.Others----Vigabatrin, Trimethadone.

VI.**EXPLAIN IN DETAIL**

1. Classify anticonvulsants with examples, Explain the drugs of choice in Grandmal.
2. What are the Neuro transmitters in CNS, Classify with examples, explain their mechanism of actions.