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Subject Name:Pharmacotherapeutics **Subject Code: 20224**

FImportant Instructions to examiners:

1) The answers should be examined by key words and not as word-to-word as given in the model answer scheme.
2) The model answer and the answer written by the candidate may vary but the examiner may try to assess the understanding level of the candidate.
3) The language errors such as grammatical, spelling errors should not be given more Importance (Not applicable for subject English and Communication Skills.
4) While assessing figures, the examiner may give credit for principal components indicated in the figure. The figures drawn by candidate and model answer may vary. The examiner may give credit for any equivalent figure drawn.
5) Credits may be given step wise for numerical problems. In some cases, the assumed constant values may vary and there may be some difference in the candidate's answers and model answers.
6) In case of some questions credit may be given by judgement on part of the examiner of relevant answers based on the candidate's understanding.
7) For programming language papers, credit may be given to any other program based on an equivalent concept.
8) As per the policy decision of Maharashtra State Government, teaching in English/Marathi and Bilingual (English + Marathi) medium is introduced in the first year of AICTE diploma Programme from academic year 2021-2022. Hence if the students write answers in Marathi or bilingual language (English +Marathi), the Examiner shall consider the same and assess the answer based on matching of concepts with model answers.

Q. No	Sub No.	Answers	Marking Scheme
1.		**Answer any SIX of the following:**	30
	a.	**Explain the clinical manifestation and pharmacological and non-pharmacological management of diabetes Mellitus?** **Marking scheme** **Clinical manifestation (0.5x2=1M)and pharmacological management(0.5x5=2.5M)and non-pharmacological management of diabetes Mellitus (0.5x3=1.5M)** **Answer** **Clinical manifestation** 1. Hyperglycemia 2. Glycosuria 3. Polyurea 4. Polydipsia 5. Polyphagia 6. Weakness in body due to less use of glucose 7. Progressive loss of weight	5M

8. Ketoacidosis
9. Blurred vision
10. Tingling or numbness in the hands or feet.
11. Very dry skin.
12. Sores that are slow to heal.
13. Recurrent urogenital infection.
14. It may also result in mood changes.

Pharmacological management of diabetes Mellitus

Insulin

All type I patients require insulin for their survival. Insulin may be categorized based on its time activity profile as:

- Ultra-short acting
- Short acting
- Intermediate acting
- Long acting insulin includes Lantus (Insulin Glargine), Levemir (Insulin detemir), Tresiba (Insulin degludec) made by recombinant DNA technology. Humalog (insulin lispro) and NovoLog are short acting insulins which is given in combination with a long acting insulin.

Oral Hypoglycemic Agents

Following categories of the drugs can be used orally for type 2 diabetes patients.

1. **Biguanides:** E.g. **Metformin**.
    - Metformin is recommended as the first line treatment in type 2 diabetes.
    - The recommended starting **daily dose is 500 mg** after meals, which is increased by 500 mg every two weeks until desired therapeutic goals are achieved or **maximum daily doses (2500 mg)** are reached.
    - It can be used in combination with any other oral or injectable antihyperglycemic agents.
    - As monotherapy, it rarely produces hypoglycemia.
    - It is advisable to stop metformin at least 24 hours before major surgery or use of radiocontrast media.
2. **Sulphonylureas:**

- e.g., **Glibenclamide (2.5 to 15 mg/day)**, **glipizide (2.5 to 40 mg/day)**, gliclazide (40 to 320 mg/day) and glimepiride (1 to 6 mg/day).
- The sulphonylureas act by binding to specific sulfonylurea receptors on pancreatic ß cells and increase insulin secretion.
- Therapy should be started with the lowest effective dose and increase every two weeks until desired control or maximal dosage is reached.
- They are preferably given 15 to 30 minutes before the meal.

3. **DPP-4 (Dipeptidyl Peptidase) inhibitors (Gliptins)**:
   - e.g. **Sitagliptin (100mg OD)**, vildagliptin, saxagliptin, linagliptin, teneligliptin and gemigliptin.
   - These agents act by inhibiting the enzyme dipeptidyl peptidase-4. They are best used in combination with metformin as a second line of therapy. They do not cause hypoglycemia Pioglitazone is an insulin sensitizer. It also inhibits hepatic glucose output. The dose is when used as monotherapy.

4. Thiazolidinediones (Glitazones):
   - **Pioglitazone** ranges from **7.5 to 30 mg once a day**. The action is visible from 2-4 weeks of starting therapy and the maximum effect is observed after 8-12 weeks. Its combination with insulin should be done with caution. Adequate contraceptive advice should be given to women using pioglitazone because it may enhance ovulation.

5. SGLT2 inhibitors (Sodium Glucose Transporter 2 Inhibitors):
   - eg. **Canagliflozin (100mg OD)**, dapagliflozin (5mg OD) .
   - They act by inhibiting SGLT 2 located on the proximal convoluted tubule of the kidney causing glycosuria. These agents reduce blood glucose levels, blood pressure and weight. Also, these agents have cardiovascular benefits over and above their glucose lowering effects

6. **Alpha Glucosidase Inhibitors:** eg. **Acarbose (50 mg orally 3 times a day)** , miglitol and voglibose
   - Alpha-glucosidase inhibitors act by competitively inhibiting alpha-glucosidase in the small intestine brush border, decrease

intestinal glucose absorption and reduce postprandial hyperglycemia. Hence, these agents are especially useful in decreasing postprandial glucose levels.

- They can be combined with all other antihyperglycemic agents. AGI must be ingested with the first bite of food, as the drug must be present in the small intestine with the food for proper effect. If hypoglycaemia results from AGI containing combination therapy, treatment should be with oral glucose rather than sucrose.

7. **Non-sulfonylurea Secretagogues (Glinides):** e.g. **Repaglinide (6 mg/day)** and nateglinide.
   - These are non-sulfonylurea insulin secretagogues. They are absorbed rapidly (0.5-1 hr) and have a short half life (< 1 hr). They result in rapid but brief release of insulin. They are useful in managing postprandial hyperglycemia. They have to be administered with each meal.

Combination Therapy: It has been observed that combination therapy is more beneficial in type 2 diabetic patients. Insulin requirement may be reduced when combined with oral agents like sulphonylureas, acarbose, metformin, troglitazone and repaglinide**.**

Non-pharmacological management of diabetes Mellitus

- Maintain normal body weight.
- Physical exercise - it improves insulin sensitivity.
- Avoid risk factors such as smoking, stress, hypertension, alcohol etc.
- Monitor blood glucose levels.
- Adopt personal hygiene to avoid infections.
- Take a high protein diet and avoid fat and carbohydrate diets.
- Do not eat sweet food.
- Boiled and steamed food to be eaten.
- Avoid alcohol intake.
- Ample amount of water should be taken daily.

	b.	**Write scope and objectives of pharmaco-therapeutics?** **Marking scheme** **Scope of pharmaco-therapeutics(0.5x5=2.5 M) and objectives of pharmaco-therapeutics(0.5x5=2.5 M)** **Answer** **Scope of Pharmacotherapeutics:** ● The goal of pharmacotherapeutics is to provide the information and skills required to contribute to the safe and effective use of medications. ● It briefly discusses pathophysiology and mainly treatments of many diseases. Pharmacotherapeutics aid in understanding the pathophysiology and management of common disorders. ● Knowledge of Pharmacotherapeutics (PT) is necessary for rational prescription. ● Pharmacotherapy knowledge is responsible for ensuring the safe, appropriate, and cost-effective use of medicines for direct patient care. ● Pharmacotherapeutics ensure that drugs are used correctly and rationally. ● Avoid and reduce adverse drug reactions and toxicity by applying PT principles. ● Maintaining drug costs at an optimum level and still providing quality and effective products, PT knowledge is required. ● With the help of Pharmacotherapeutics, we can keep drug costs low while still providing high- quality, effective products and ensuring patient compliance. Pharma industries: A pharmacologist may work in several departments in the industries as - ● Medical advisor: He can help with a variety of things as a medical advisor including the analysis of population health, evaluation of primary care services, planning of services, advice on effective prescribing and education of general practitioners. ● Medical transcription: The process of transcribing or converting voice-recorded reports as dictated by physicians into text format. ● Medico-marketing: Business of advertising or promoting the sale of pharmaceuticals.	**5M**

		• Product management: This plays an important role in all phases of the product life cycle - introduction, growth, saturation and decline or stable phase. • Contract research organisation (CRO): These provide clinical study and clinical trial support for drugs &/or medical devices. • Training: A pharmacologist may provide training to medical representatives and physicians. Special domains: A pharmacologist may also work in special domains like Pharmacovigilance, Pharmacoeconomics, Pharmacoepidemiology and Chronopharmacology. • Pharmacovigilance: It is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine/vaccine related problem. • Pharmacoeconomics : It refers to the science that compares the value of one drug over another • Pharmacoepidemiology: It studies the use and effects of drugs in large population: • Chronopharmacology: It is the science concerned with the variations in pharmacological actions of various drugs over biological timings **Objectives of Pharmacotherapeutics** • To understand the pathophysiology of selected ailments and different disease states along with the drug therapy. • To know about therapeutic strategies to treat the disease. • To eradicate the controversies in drug therapy. • To prepare a treatment plan. • To avoid and reduce adverse drug reactions and toxicity. • To find a patient specific parameter to start the treatment. • To maintain drug cost at an optimum level and still provide quality and effective products. • To ensure patient compliance. • To ensure proper and rational use of drugs.	
	c.	**What is Hyperlipidemia ? Explain Etiopathogenesis of it.** **Marking scheme: Definition 1M and Etiopathogenesis 4M**	**5M**

Answer

Definition of Hyperlipidemia

Hyperlipidemia (also known as dyslipidemia) is a disorder of lipoprotein metabolism in which elevated level of total cholesterol is seen with increase in LDL and/or triglyceride level and decrease in HDL level that if not treated to restore, leads to cardiovascular disease.

Etiopathogenesis of Hyperlipidemia:

- Presence of disorders or diseases like diabetes, obesity, hyperthyroidism, chronic renal failure and alcoholism can cause secondary dyslipidemia.
- Human liver is able to produce the required amount of lipid on its own for normal body functions. Dietary fats and lipids are excessive and unnecessary. If more amounts of saturated fat, trans fat, refined carbohydrates and sugar are consumed and not utilized, it causes hyperlipidemia.
- Many drugs can precipitate hyperlipidemia as their side effect or withdrawal symptom for example antihypertensive like diuretic and ß-blockers, oral contraceptives, anti-psychotics, ciclosporin, corticosteroids.
- Lipid and fat metabolism in the body is governed by many processes. Major role in this process is the LDL receptor that removes excess amounts of LDL from serum and prevents accumulation of lipid molecules in blood vessels.
- If the gene that regulates the receptor function gets mutated, LDL receptor function decreases leading to failure of cholesterol clearance and lipid level increases in blood causing hyperlipidemia.
- If the amount of lipid is excessive, then even if the receptor expression gene is normal, the efficiency of clearance decreases due to desensitization of receptors. This causes accumulation of lipids in blood.
- Apart from this certain drugs affect the feedback mechanism for cholesterol synthesis and/or decreases bile acid synthesis. Thus either increases cholesterol synthesis or decreases its solubilisation through bile and causes hyperlipidemia.
- As mentioned earlier, the liver can produce all types of lipids and fats in the required amount in the body. So the dietary fats and lipids if consumed in

		excess amount and/or not utilized by the person can remain accumulated and not excreted due to limited capacity of systems.	
	d.	**Explain clinical manifestation of Epilepsy.Describe its pharmacological and non -pharmacological epilepsy.** **Marking scheme** **clinical manifestation of Epilepsy (0.5x2=1M) , pharmacological management (0.5x6=3M) and non -pharmacological management epilepsy(0.5x2=1M).** **Answer** **Clinical manifestation of Epilepsy** ● Temporary confusion. ● A staring spell. ● Stiff muscles. ● Uncontrollable jerking movements of the arms and legs. ● Loss of consciousness or awareness. ● Psychic symptoms such as fear, anxiety. ● confused speech. ● Anxiety. **Pharmacological treatment of Epilepsy** **Antiepileptic drugs for different types of seizures**	**5M**

Seizure type	**First-line treatment**	**Second-line treatment**
Generalised seizures		
Tonic clonic	Sodium valproate	Lamotrigine
Absence	Ethosuximide, Sodium valproate	Clonazepam, Lamotrigine
Myoclonic	Sodium valproate, Clonazepam	Levetiracetam, Acetazolamide Topiramate
Atonic	Clonazepam, Clobazam	Lamotrigine, Carbamazepine, Phenytoin, Acetazolamide, Topiramate
Partial seizures	Carbamazepine,	Topiramate, Sodium valproate Clobazam, , Zonisamide,

	Oxcarbazepine, Levetiracetam	Pregabalin, Phenytoin, Gabapentin, Lamotrigine, Lacosamide

Antiepileptic drugs

Drugs that are effective in seizure reduction accomplish this by a variety of mechanisms

1. Enhancement of inhibitory GABAergic impulses, or
2. Interference with excitatory glutamate transmission.

1. <u>By enhancing the inhibition</u>

A.Barbiturates –Phenobarbital

B.Benzodiazepines- clonazepams , Lorazepams, clobazam

C.Cyclic GABA- Gabapentin

A. Barbiturates – Phenobarbital acts on GABA receptors, increasing synaptic inhibition. This has the effect of elevating seizure threshold and reducing the spread of seizure activity from seizure focus. Phenobarbital may also inhibit calcium channels , resulting in a decrease in excitatory transmitter release The primary use for phenobarbital in epilepsy is in **treatment of status epilepticus.** adverse effects of sedation, cognitive impairment, and potential for osteoporosis.

B. Benzodiazepines-Diazepam, clonazepams Benzodiazepines **bind to GABA inhibitory receptors to reduce firing rate.** Effective in short-term treatment of all seizures; used often in the emergency room to stop a seizure, **particularly status epilepticus** Tolerance develops in most within a few weeks, so the same dose has less effect over time.Valium can be given orally, as an injection, in an IV or as a rectal suppository. Side effects include tiredness, unsteady walking, nausea, depression, and loss of appetite. In children, they can cause drooling and hyperactivity.

C. Cyclic GABA- Gabapentin ,its analogues **Pregabalin** It works by showing a **high affinity for binding sites throughout the brain and** cross the Blood brain barrier (lipophilic cyclohexane ring.) It seems **to inhibit the release of excitatory neurotransmitters in the presynaptic area; the primary** use for

phenobarbital in epilepsy is in **treatment of status epilepticus.** adverse effects of sedation, cognitive impairment, and potential for osteoporosis,

2. **By reducing the excitation.**

A. **Hydantoin: Phenytoin**, Fosphenytoin They show their action by blocking sodium channels and inhibition of the generation of repetitive action potentials. Side effect -Depression of the CNS occurs Gingival hyperplasia may cause the gums to grow on teeth. Long term use may lead to development of peripheral neuropathies and osteoporosis.

B. **Iminostilbene: Carbamazepine** reduces the propagation of abnormal impulses in the brain by blocking sodium channels, thereby inhibiting the generation of repetitive action potentials in the epileptic focus and preventing their spread.Carbamazepine is effective for treatment of partial seizures and secondarily generalized tonic-clonic seizures as well as trigeminal neuralgia (facial nerve pain)and in bipolar disease Adverse effect -usually due to skin rash, gastrointestinal disturbances or hyponatremia ,ataxia, dizziness, blurred vision and diplopia.

C. **Ethosuximide:** Ethosuximide is used **to control absence (petit mal) seizures in patients with epilepsy.** These drugs **block Ca channel and prevent Ca influx** The most commonly encountered adverse effects - Behaviour disorders, anorexia, fatigue, sleep disturbances and headaches may also occur.

D. **Oxazolidinedione Derivatives:** Oxazolidinedione derivatives like; **trimethadione**, paramethadione are specifically used in the treatment of petit mal epilepsy.Inhibition of voltage gated calcium channel Sedation and blurring of vision are common side effects.

E. **Valproate, valproic acid (Depakene, Depakote):** Used to treat partial, absence, and generalized tonic-clonic seizures enhancing level of GABA (γ aminobutyric acid) in the CNS, blocking Ca channels (voltage-gated channel) Common side effects include dizziness, nausea, vomiting, tremor, hair loss, weight gain, depression in adults, irritability in children, reduced attention, a decrease in thinking speed, bone thinning, swelling of the ankles, irregular menstrual periods. Should not be taken if pregnant.

		Non -Pharmacological Treatment ● Avoid any known seizure trigger . ● Avoid alcohol drinking ● Know when seizures are most likely to occur ● Get enough sleep ● Be healthy ● Manage stress ● VNS (Vagus nerve stimulation) ● Dietary modification consists of a ketogenic diet.	
	e.	**What is Tuberculosis ?Explain etiopathogenesis and clinical manifestation of Tuberculosis** **Marking scheme: Definition 1M ,etiopathogenesis 2M and clinical manifestation 2M** **Answer** **Definition of Tuberculosis** It is an infectious bacterial disease caused by Mycobacterium tuberculosis, which most commonly affects the lungs but they can also damage other parts of the body. It is transmitted from person to person via droplets from the throat and lungs of people with the active respiratory disease. **Etiopathogenesis of Tuberculosis** ● Tuberculosis results almost exclusively from inhalation of airborne particles (droplet nuclei) containing Mycobacterium Tuberculosis bacteria. ● Coughing, singing, and other forced respiratory movements by infected people. ● Sputum contains a significant number of organisms ● Inhalation of droplet nuclei containing the causative microorganism Mycobacterium tuberculosis reach the alveoli of the lungs. ● This may lead to the development of infection depending on the virulence of mycobacteria and the immunity of the person. ● Macrophages help in the phagocytosis of the bacilli and eliminate it.	**5M**

		• In case the bacilli persist, they divide slowly in macrophages, and lysis of the macrophages leads to the release of the bacilli. • The lymphocytes and macrophages lead to the formation of granulomatous lesions, also called tubercles. The lesions may undergo fibrosis, calcification, and heal. • A few other lesions may undergo progression. • The bacilli are transported to the regional lymph nodes during the early stages of infection. • The bacilli may spread to other parts of the body through the bloodstream and lymphatic system. They divide in spleen, kidneys, bone, meninges, and apical region of lungs. **Clinical Manifestations Tuberculosis** • A bad cough that lasts 3 weeks or longer • Weight Loss • Coughing up blood or mucus • Loss of appetite • Weakness or fatigue • Fever • Night sweats • Chest pain, or pain with breathing or coughing • Chills	
	f.	**Define and Explain types, etiopathogenesis of peptic ulcers?** **Marking scheme:(definition 1 M, Types of peptic ulcer explanation 1 M and Etiopathogenesis 3M)** **Answer :** **Definition of peptic ulcers** Peptic ulcer diseases are ulcers (sores) which occur in the lining of the stomach (gastric ulcer) &/or small intestine (duodenal ulcer) due to exposure to gastric acid. **Types of peptic ulcers** There are three common forms of peptic ulcers: 1) Gastric ulcer: ulcers inside the stomach. 2) Esophageal ulcer: ulcers inside the esophagus.	**5M**

		3) Duodenal ulcer: ulcers in the upper part of the small intestine i.e., duodenum. **Etiopathology of Peptic ulcer.** ● H. pylori infection, several Nonsteroidal anti-inflammatory drugs, stress, viral infections, Crohn's Disease, Zollinger-Ellison syndrome / Gastrinoma and are the main causes of peptic ulcer. ● Due to H. pylori infection, H. pylori bacterium has the ability to produce enzyme urease. that breaks down urea into ammonia and CO_2 protects the organism by neutralizing the acidic gastric environment. ● Bacterial lipopolysaccharide attracts inflammatory cells to the mucosa. ● A bacterial platelet-activating factor promotes thrombotic occlusion of surface capillaries. ● Mucosal damage allows leakage of tissue nutrients in the surface microenvironment, sustaining the bacillus. ● Damage of the protective mucosal layer. The epithelial cells are exposed to the damaging effect of acid-peptic digestion. ● Inflammation of the gastric mucosa. ● Chronically inflamed mucosa more susceptible to acid- peptic injury and prone to peptic ulceration. ● Ulcers occur at sites of chronic inflammation . Eg - Antrum ● The secretion of prostaglandin normally protects the gastric mucosa. ● NSAIDs **block prostaglandin synthesis by inhibiting the COX-1 enzyme,** resulting in decreased gastric mucus and bicarbonate production and a decrease in mucosal blood flow.	
	g.	**Describe Pharmacological and non -pharmacological management of Hepatitis .** **Marking scheme:** **(Non -pharmacological management of Hepatitis 0.5 X 4=2M, Pharmacological management (1x3=3M)** **Answer** **Non-pharmacological management of Hepatitis:** ● Get the vaccines for hepatitis A and hepatitis B (currently, vaccines are not	**5M**

available for hepatitis C).

- Practice good personal hygiene (hand-washing with soap and water).
- Avoid drinking contaminated water.
- Avoid eating raw or undercooked food, shellfish and oyster.
- Avoid oily and spicy food.
- Do not share needles, razors, toothbrushes etc.
- Do not drink alcohol.
- Use a condom during sex.
- Avoid hepatotoxic drugs such as paracetamol.
- Rest if the patient feels exhausted.

Pharmacological management of Hepatitis:

Hepatitis A

- People who are at risk of getting HAV should receive serum Immune Globulin (IG) and/or the hepatitis A vaccination. Vaccination gives protection against hepatitis A for about 20 years. The immunoglobulin A (0.02 ml/kg) should be administered as a single dose.
- Drinking bottled water and avoiding fruits, vegetables and raw shellfish obtained from sewage-contaminated water may minimize the risk of infection.

Hepatitis B

- For the prevention of hepatitis B infection, two products are available: hepatitis B vaccination, which offers active immunity, and hepatitis B immunoglobulin (HBIg), which provides temporary passive protection. Immunization against viral hepatitis aims to prevent short-term viremia, which can progress to infection transmission, clinical illness, and chronic HBV infection.
- Vaccine side effects include discomfort at the injection site, headache, weariness, irritability, and fever.

Chronic Hepatitis B

- The first approved agent for the treatment of chronic hepatitis B was interferon. Interferon alpha-2b (5 million IU is administered subcutaneously daily or 10 million IU dose thrice weekly) for a duration ranging from 16 weeks to 12 months. The side effects seen due to interferons are fever, fatigue, headache, myalgia, nausea, diarrhea, anorexia, anemia, leukopenia, and thrombocytopenia
- Antiviral drugs for hepatitis B includes Lamivudine , Adefovir , Entecavir
- Lamivudine helps in blocking hepatitis B viral replication. It is given at a dose of 100 mg orally daily for 52 weeks. The side effects are headache, malaise, fatigue nausea, vomiting, diarrhoea, neuropathy, cough, congestion, and musculoskeletal pain. Neutropenia, anaemia, thrombocytopenia, and pancreatitis are also seen A major concern with lamivudine treatment is the development of hepatitis B viral mutation and drug resistance.
- Adefovir has antiviral activity against hepatitis B and is administered at 10 mg daily for 48 weeks. The side effects are nausea, diarrhoea, vomiting, dyspepsia, headache, weakness, pruritus, rashes, and nephrotoxicity.
- Entecavir is given at a dose of 0.5 mg orally once a day.

Hepatitis C

- Immunoglobulins are no longer recommended for prophylaxis of hepatitis C because they are not effective in preventing it.
- A vaccine for hepatitis C was developed but was not found effective due to the rapidly mutating virus. The transmission of hepatitis C via transfusion has been controlled by following various screening procedures.
- The sexual transmission of hepatitis C can be prevented by using barrier precautions like condoms.
- A person infected with hepatitis C should avoid sharing items such as toothbrushes, razors, and nail cutters with family members.
- Chronic hepatitis C infections are treated with peginterferon plus ribavirin. Ribavirin shows hemolytic anemia, insomnia, depression, irritability, allergy

		like rashes and purities as the side effects. Ribavirin is embryo toxic and highly teratogenic, so it should not be used in pregnant women or in men with pregnant female partners. **Hepatitis D** ● This can be prevented by vaccinating people with the hepatitis B vaccine. **Hepatitis E** ● There is no specific treatment capable of altering the course of acute hepatitis E. ● As the disease is usually self-limiting, hospitalization is generally not required. ● Hospitalization is required for people with Fulminant hepatitis.liver function impairment	
2.		**Answer any TEN of the following:**	**30**
	a.	**What is glaucoma? Explain clinical manifestation of glaucoma?** **(Glaucoma 1 mark, clinical manifestations 2 marks)** **Ans:** Glaucoma is defined as a disease condition of the eye in which the optic nerve is damaged which is mostly associated with increase in intraocular pressure. It may cause various degrees of loss of vision and blindness. **Clinical manifestations of Glaucoma** ● Redness of eye ● Fatigue of organs of vision ● Head pain ● Intense eye pain ● Vision loss ● Lacrimation ● Rainbow-colored halos around lights. ● Low vision, blurred vision, narrowed vision (tunnel vision) or blind spots. ● Nausea and vomiting.	**3M**

	b.	**Explain pharmacological management of iron deficiency anaemia. (3 marks)** **Oral iron therapy-** ● Iron is available in ferrous and ferric forms. The ferrous form of iron is economical, safe as well as an effective form of oral iron therapy. Ferrous sulphate, ferrous gluconate and ferrous fumarate are used in tablet and syrup form. The elemental iron present in the oral preparations is helpful in treatment of iron deficiency anemia. ● The standard treatment is **ferrous sulphate 200 mg 2 to 3 times a day.** ● Side effects are on the gastrointestinal tract. Nausea, vomiting, abdominal pain, black stools and constipation may be seen. **Parenteral iron therapy -** ● When iron is administered parenterally, it has no added advantage over oral therapy. So, this therapy should be reserved for patients who cannot tolerate oral iron therapy or show improper absorption of iron. ● **Iron dextran (100mg I.V. < 50 mg/min) -** This is a complex of ferric oxide and dextran. Once it is injected as intravenous infusion or slow intravenous injection or by intramuscular injection, the iron dextran complex is separated by the reticuloendothelial system in the body. **A test dose of 0.5 ml containing 25 mg should be given before initiating the therapy to check for adverse reactions**. Most reactions occur during the initial administration and range from mild reactions to life-threatening anaphylactic shock. The mild reactions are transient and may be seen as dyspnoea, headache, nausea, vomiting, flushing, itching, urticaria, fever, chest pain or abdominal and back pain. A patient who has not shown anaphylactic shock during the test dose may even show it during therapy. The adverse systemic reactions may be seen later after one or two days of iron dextran therapy as myalgias and arthralgias. ● **Iron sucrose (1000 mg divided in three doses/ week) :** This is a complex of **ferric hydroxide and sucrose**. Once administered, this complex is dissociated by the reticuloendothelial system of the body. This is administered to patients with kidney issues.	**3M**

		• **Ferric gluconate (125 mg IV infusion over 1 hr)**: The FDA approved sodium ferric gluconate complex in sucrose in the year 1999 for the treatment of iron deficiency anemia in patients undergoing haemodialysis and receiving erythropoietin therapy. • **Red cell transfusion** : This therapy may be required in patients who require immediate medical relief in blood loss. Also, this transfusion therapy is reserved for patients with symptoms of cardiovascular instability with anemia.	

	c.	**Explain etiopathogenesis of depression. (3 marks)**	**3M**

Etiopathogenesis of Depression:

- It is likely that genetic, hormonal, biochemical, environmental, and social factors all have some role in determining an individual's susceptibility to developing the disorder.
- Normal physiology of a patient's mood, perception, emotion and behavior focuses majorly on neurotransmitters in the brain.
- Serotonin is involved with mood, happiness, anxiety, and sleep induction.
- Norepinephrine in the brain helps regulate alertness, mood, functions in dream sleep, and maintains arousal (alertness or waking up).
- Dopamine in the brain regulates reward and motivation which could explain the loss of interest in patients with depression.
- There is a deficit in the concentration of the brain norepinephrine, dopamine, and/or serotonin resulting in depression. different hypothesis mentioned are as follows,
  - **Monoamine Hypothesis:**
    - The monoamine hypothesis of depression suggests that depression is related to the decrease in amount and functions of cortical and limbic serotonin (5-HT), norepinephrine (NE) and dopamine (DA).
    - In the normal brain, monoamine neurotransmitters are released and bind to receptors on the postsynaptic neuron. Transmission is terminated by reuptake of the transmitter.
    - In depression, the decreased concentration of monoamine at synaptic sites produces a mood disorder.
    - Treatment with reuptake inhibitors blocks the reuptake sites and increases the concentration of monoamine neurotransmitters in the synaptic cleft, so more are available to bind to receptors on the neighbouring neuron. This restores the mood.
  - **Receptor Sensitivity Hypothesis:**
    - The 5-HTa receptor sensitivity hypothesis was suggested to explain the time gap. According to this hypothesis, depression develops due to

abnormally increased somatodendritic 5-HTa, auto-receptor function, and antidepressants work by down-regulating the presynaptic 5-HTα, receptor.Suicidal and depressed patients have increased 5-HTa, receptors.

❖ **Permissive Hypothesis:**

➢ The control of emotional behavior results from a balance between noradrenaline and serotonin (5-HT). According to this theory, both the manic phase (psychosis) and the depressive phase of bipolar disorder are characterized by low central serotonin function.

➢ The permissive hypothesis postulates that low levels of serotonin permit abnormal levels of noradrenaline to cause depression or mania On the other hand, if the level of serotonin falls and the level of noradrenaline becomes abnormally high, the patient becomes manic.

❖ **Serotonin-only Hypothesis:**

➢ This hypothesis emphasizes the role of serotonin in depression and down plays noradrenaline. This hypothesis suggests that depression is caused by the low levels of serotonin. Serotonin is a neurotransmitter produced in specific neurons in the brain and they are called "Serotonergic neurons" because they produce serotonin.

❖ **Electrolyte Membrane Hypothesis:**

➢ Electrolytes also play an important role in the stabilization of mood. According to this hypothesis, the altered level of electrolytes may cause depression. Hypocalcemia may be associated with mania. Hypercalcemia is associated with depression.

❖ **Neurotrophic Hypothesis:**

➢ Depression appears to be associated with a drop in brain-derived neurotrophic factor (BDNF) levels in the cerebrospinal fluid and serum, as well as with a decrease in tyrosine kinase receptor B activity.

	d.	**Enlist the clinical manifestation of Covid-19.** **Making scheme: (0.5 X 6 = 3 marks)** The typical symptoms of Covid - 19 are ● Fever ● Sore throat ● Dry cough ● Fatigue ● Tiredness ● Loss of taste or smell ● Diarrhoea ● Aches and pain ● Headache ● and, in severe cases, Dyspnoea. Many infections are asymptomatic, especially in children and young adults, whereas older people and/or people with co-morbidities are at a higher risk of severe disease, respiratory failure, and death. The incubation period is 5 days; severe disease usually appears 8 days after the onset of symptoms, and critical disease and death occur after around 16 days.	**3M**

	e.	**Describe pharmacological management of hypertension.** **(0.5 X 6 = 3 marks)** The various drug classes which are used in the treatment of hypertension include: ● Diuretics e.g. Furosemide (20-80 mg /day), Chlorthalidone, Indapamide ● Beta blockers e.g., Propranolol (160-240 mg/day), timolol, metoprolol ● Calcium channel blockers e.g. Amlodipin (2.5 to 10 mg/day) Diltiazem , verapamil ● ACE inhibitors e.g., Captopril, enalapril (5-40 mg/day) ● Aldosterone antagonists e.g., spironolactone (25-50 mg/day ● Alpha adrenergic blockers e.g., terazosin, prazosin (2-20 mg /day) ● Combined alpha and beta blockers e.g., carvedilol, labetalol ● Direct vasodilators e.g., minoxidil (10-40 mg /day), hydralazine. **Diuretics:** ● Thiazide diuretics (e.g., chlorthalidone) are used as first line treatment of essential hypertension. Diuretics act by increasing the excretion of sodium and thereby water excretion is increased. This leads to decrease in blood volume thereby decreasing the blood pressure. ● Adverse effects of thiazide diuretics include hypokalaemia, hyperuricemia, glucose intolerance, sexual dysfunction, dyslipidemia, hyponatraemia, hypermagnesemia, skin rash and photosensitivity. ● The other diuretics which are used are loop diuretics (furosemide) and potassium sparing diuretics (spironolactone, amiloride). **Beta blockers**: ● Beta blockers competitively block catecholamine neurotransmitters thereby reducing the heart rate, venous return, and cardiac output. This helps in reducing the blood pressure. ● Adverse effects - The adverse effects of beta blockers include effects due to blockade of β_1 receptors and effects due to blockade of β_2 receptors. β_1 blockade may lead to left ventricular failure, conduction problems in heart	**3M**

and bradycardia. The β_2 receptors blockade effects include bronchoconstriction, claudication and cold extremities.

- Withdrawal symptoms may be seen on abrupt cessation of beta blockers. Also, the stopping of beta blockers over a period of 4 to 8 days may show overshoot hypertension, so the beta blockers should be stopped slowly over a period of a few months.

ACE inhibitors

- ACE inhibitors inhibit the activity of ACE (Angiotensin Converting Enzyme) which decreases the production of angiotensin-II which is a potent vasoconstrictor. They have good efficacy as antihypertensive monotherapy similar to diuretics and beta blockers.
- Adverse effects include hypotension, hyperkalaemia, cough, angioedema.

Aldosterone antagonists

- Spironolactone is a specific aldosterone antagonist which is used either alone or in combination with thiazide diuretics.
- Adverse effects - This may show hyperkalaemia. Also, it should not be given in cases of renal insufficiency. Other side effects include gynaecomastia, impotence and menstrual problems.

Calcium channel blockers

- Calcium antagonists act by closing the calcium ion channels in the smooth muscles of blood vessels. This reduces the contractility and tone of the vascular muscles. There are three classes of calcium channel blockers - benzothiazepines (e.g., diltiazem), alkylamines (e.g., verapamil) and dihydropyridine (e.g., Amlodipine, felodipine, and nicardipine).
- Adverse effects - headache, vasodilation, hypotension, oedema.

Alpha adrenergic blockers:

- Alpha adrenoreceptor antagonists lower the blood pressure by acting on the alpha-1 receptors present in the walls of the blood vessels. These drugs

		decrease peripheral resistance and cause vasodilation without any effect on the cardiac output or heart rate. **Direct vasodilators** ● These agents, as the name suggests, act directly on blood vessels to relax them. This helps in treating hypertension but these drugs cannot be used as monotherapy. They should be used with diuretics and beta blockers. The drugs include hydralazine, minoxidil, diazoxide and nitroprusside. These drugs are fast acting to treat hypertension. ● Nitroprusside is an instant acting vasodilator and is used in almost all cases of hypertensive emergencies. ● Adverse effects- The adverse effects of these drugs are mainly due to direct vasodilation effects like headache, dizziness, tachycardia. These drugs cause oedema due to sodium and water retention. Hydralazine may cause lupus-like syndrome. Minoxidil causes hypertrichosis which makes it difficult to be used in women and cardiac effusion.	
	f.	**What are the three stages of ALD (Alcoholic Liver Disease)?** **(each stage 1 mark)** The three stages of ALD are: 1. **Alcoholic fatty liver** - This is the first stage of the disease in which fat begins to accumulate around the liver. Drinking a large volume of alcohol mobilises peripheral fat and increases fat synthesis in the liver. There is an accumulation of triglycerides in the liver. This stage is often reversible if the individual stops alcohol. 2. **Alcoholic hepatitis** - In this stage, alcohol abuse causes liver inflammation. This can occur after many years of heavy drinking. If the individual abstains from alcohol on a long-term basis, alcoholic hepatitis is usually reversible. 3. **Cirrhosis:** This occurs when the liver has been inflamed for a long time leading to scarring, fibrosis and loss of function. Cirrhosis due to alcoholism is the most severe form of the disease. The liver is scarred by alcohol abuse	**3M**

		and the damage cannot be reversed. Cirrhosis can result in liver failure.	
	g.	**Explain etiopathogenesis of rheumatoid arthritis. (3 marks)** Underlying causative factors are not clear for rheumatoid arthritis but following risk factors are associated with it. ● Hormones/Gender: It has been observed that females are more likely to develop rheumatoid arthritis than males ● Age: RA develops with increasing age, at the peak of 35-50 years of age ● Genetic factors: Genetic factors contribute to 53 -65 % of developing risk factors for RA. The HLA (Human Leukocyte Antigen) - DR4 allele is associated with both development and severity of RA. ● Cigarette smoking: Smokers are more likely to have extra-articular manifestations and to experience treatment unresponsiveness. ● Stress: Stress also affects RA onset and its progression. Chronic presence of minor stressors like daily hassle, work and relationship stress, financial pressure; rather than more stressful events may affect immune response and RA activity. ● Pathological changes in development of RA include infiltration of a variety of inflammatory cells into the joint. Synovial fibroblast becomes proliferated with an influx of inflammatory cells like T-cells, B-cells, macrophages, and plasma cells. Cytokines like (TNF)-alpha, interleukin-1, interleukin-6 and GM-CSF are released by these cells that release proteolytic enzymes and ultimately destroy bone and cartilage.	**03**
	h.	**Discuss prevention of antimicrobial resistance. (any 6 points, 3 marks)** The strategies for overcoming drug resistance are ● Administration of drugs in proper concentration ● Avoid two or three different drugs simultaneously ● Adequate therapy ● Use of antibiotics only when prescribed by certified health professional	**3M**

		● Patient compliance ● Neither use or share leftover medicines ● Prevent infections by regularly washing hands ● Avoid close contact with infected people and practise safe sex ● Take vaccinations on time ● Prepare food hygienically. Follow the WHO Five Keys to Safer Food (keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials). Choose foods that have been produced without the use of antibiotics for growth promotion or disease prevention in healthy animals ● Ensure a national action plan to tackle antibiotic resistance ● Administer antibiotics to animals only under veterinary supervision. ● Vaccinate the animals to avoid use for antibiotics. ● Establishing an infection prevention and control committee (IPC). ● Effective diagnosis and treatment of infection. ● Rational antimicrobial use. ● Surveillance of antibiotic resistance and antibiotic use. ● Improving the antimicrobial quality and supply chain.	
	i.	**Explain pharmacological management of Parkinson's disease. (3 marks)** ● Antiparkinsonian drugs can only help to reduce the symptoms and improve the quality of life. ● Two categories in the treatment are: 1. To enhance dopamine activity; 2. To depress cholinergic overactivity. **1. Drugs affecting brain dopaminergic system:** a. Dopamine precursor- Levodopa 300 mg/day b. Peripheral decarboxylase inhibitors-Carbidopa 25 to 100 mg, Benserazide c. Dopaminergic agonists- Ropinirole 0.25 mg, Pramipexole 0.125 mg TD d. MAO-B inhibitors- Selegiline 5 mg OD.	**3M**

e. COMT (Catechol-O-methyltransferase) inhibitors- Entacapone 200 mg, Tolcapone 100-300 mg TD.

f. Dopamine facilitator- Amantadine 100-300 mg/day

2. Drugs affecting brain cholinergic system:

A. Central anticholinergics- Trihexyphenidyl (Benzhexol), Procyclidine, Biperiden

B. Antihistamines- Orphenadrine, Promethazine

Levodopa: This has been the most effective drug in the treatment of Parkinson's disease. After entry into the peripheral circulation, levodopa crosses the blood-brain barrier (BBB) where it is taken up by the dopaminergic neurons of the substantia nigra and converted into dopamine by the enzyme dopa decarboxylase, which is then released to act on dopamine receptors in the striatum.

Carbidopa is a reversible dopa decarboxylase inhibitor (DCI) that does not cross the BBB. When administered in the absence of a DC inhibitor, levodopa undergoes significant peripheral metabolism to dopamine, which is undesirable as dopamine cannot cross the BBB.

Hence, levodopa is commonly used in combination with a DCI like carbidopa or benserazide. The usual starting dose is 50 mg of levodopa with 12.5 mg of carbidopa given 3 times a day. The dose is then gradually increased till maximum benefit is achieved without serious toxicity; this may be 500–1000 mg daily in 3–4 divided doses.

Nausea, vomiting, anorexia, postural hypotension, and palpitations are some of the early adverse drug reactions of levodopa. Behavioral and CNS effects occur during prolonged treatment. Behavioral side effects include agitation, confusion, restlessness, hallucinations, delusions, and depression.

Dopamine agonists (DA) like bromocriptine are used even though they have limited efficacy. About 1/3 of the patients have a good response to these drugs and may not need levodopa for 3-5 years. Other DA agonists approved are pergolide, pramipexole, and ropinirole.

		Amantadine (a drug which releases dopamine) is used in patients with mild PD. It can also be used as an adjunct in patients who cannot tolerate levodopa. **Selegiline** is an irreversible enzyme inhibitor with relative selectivity for MAO-B. It is associated with a delay in the need for levodopa, slowed disease progression, and extended employability. **Entacapone and tolcapone** are peripheral COMT(Catechol-O-methyltransferase) inhibitors when given with levodopa and DCI formulations are useful for reducing wear-off symptoms and total daily levodopa intake. **Surgery**: Thalamotomy, pallidotomy, and deep-brain stimulation with implanted electrodes may benefit patients under 50 who suffer from severe symptoms unresponsive to drug therapy.	
	j.	**What is polycystic ovary syndrome? Mention its clinical manifestations. (PCOS 1 mark, clinical manifestations 0.5 X = 2 marks)** Polycystic ovary syndrome (PCOS) is a hormonal condition that affects a large number of women of reproductive age. Women with PCOS may have irregular or prolonged menstrual cycles or high levels of male hormone (androgen) levels. The ovaries may develop numerous small collections of fluid (follicles) and fail to release eggs regularly. It is defined as a hormonal condition in women of reproductive age and is characterised by menstrual disorders (such as oligomenorrhea, amenorrhea, menorrhagia, infertility) hyperandrogenism (which manifests as hirsutism and acne), obesity and polycystic ovaries. **Clinical manifestations:** The most common signs of PCOS are ● Infrequent, irregular, or prolonged menstrual cycles. ● Hirsutism (excess facial and body hair) ● Acne ● Oily skin and hair	**3M**

		• Hair thinning and hair loss • Darkened skin patches (acanthosis nigricans) • Weight gain • Difficulty in conception • Severe anxiety, depression and social stress.	
	k.	**Define emphysema and chronic bronchitis. Mention clinical manifestations of COPD. (each definition 0.5 mark, clinical manifestations 0.5 X4 = 2 mark)** **Emphysema** is abnormal permanent enlargement of the air spaces distal to the terminal bronchioles along with destruction of its wall. **Chronic bronchitis** can be defined as inflammation of bronchi with chronic or recurrent excess mucus secretion into the bronchial tree. **Clinical Manifestations** • Shortness of breath, after even mild forms of exercise like walking up a flight of stairs. • Wheezing, which is a type of higher-pitched noisy breathing, especially during exhalations. • Chest tightness. • Chronic cough, with or without mucus • Need to clear mucus from your lungs every day. • Frequent colds, flu, or other respiratory infections. • lack of energy. • Breathlessness. • Sore throat.	**3M**
3.		**Answer any <u>All</u> of the following:**	**20**
	a.	**What is normal value of blood pressure.** **Answer:** Normal value of blood pressure is 120/80 mmHg.	**1M**
	b.	**Define COPD.**	**1M**

		Answer: Chronic obstructive pulmonary disease is a chronic inflammatory lung disease that causes obstructed airflow from the lungs.Symptoms include breathing difficulty,cough,mucus production and wheezing. It is classified as emphysema and Chronic bronchitis.	
	c.	**Parkinson's disease caused by loss or degeneration of ……Neurons in the substantia Nigra for midbrain.** **Answer:** Dopaminergic	**1M**
	d.	**HIV stand for……** **Answer:** Human Immunodeficiency Virus	**1M**
	e.	**Salbutamol is in the treatment of……..** **Answer:** Asthma/COPD	**1M**
	f.	**Name drugs used in treatment of Malaria.** **Answer: (any two drugs)** Chloroquine,Amodiaquine,Primaquine,Bulaquine,Proguanil,pyrimethamine,trimethoprime,Dapsone,Sulfadoxine,Tetracycline,Doxycycline,Mefloquine,Quinine, Artemether,Artesunate,Atovaquone etc.	**1M**
	g.	**What is dysmenorrhea?** **Answer:** It is the term used to describe painful periods.It causes severe and frequent cramps and pain during the period.	**1M**
	h.	**What is Psoriasis?** **Answer:** Psoriasis is a chronic inflammatory dermatosis characterised by excessive keratinocyte proliferation that results into thickened scaly patches ,redness,itching and inflammatory changes in the epidermis and dermis.It most commonly affects the skin of the knee,elbows,trunk and scalp.	**1M**
	i.	**What is angina pectoris?** **Answer:** Angina pectoris is characterised by sudden severe chest pain due to the imbalance between oxygen demand by the heart and oxygen supply to the heart.	**1M**
	j.	**Hyperthyroidism is caused by……..**	**1M**

		Answer: i) Grave's disease	
	k.	**Define GERD.** **Answer:** Gastroesophageal reflux disease (GERD) is a condition in which the stomach contents leak backward from the stomach into the esophagus (food pipe). Food travels from your mouth to the stomach through your esophagus. GERD can irritate the food pipe and cause heartburn and other symptoms.	**1M**
	l.	**Sulfa drug used in the inflammatory Bowel disease include……** **Answer:** i) Sulfasalazine	**1M**
	m.	**What is synonym for Eczema?** **Answer:** Atopic dermatitis	**1M**
	n.	**PCOS stands for ……..** **Answer:** Polycystic Ovary Syndrome	**1M**
	o.	**Define Schizophrenia.** **Answer:** Schizophrenia is a serious mental disorder in which people interpret reality abnormally. Schizophrenia may result in some combination of hallucinations, delusions, and extremely disordered thinking and behavior that impairs daily functioning, and can be disabling.	**1M**
	p.	**Migraine is ……disorder.** **Answer:** iii) Neurovascular	**1M**
	q.	**Name causative organism of scabies.** **Answer:** Sarcoptes scabies	**1M**
	r.	**GAD stands for ……** **Answer:** Generalized Anxiety Disorder.	**1M**
	s.	**The use of at least five drug daily by an individual is…….** **Answer:**i) Polypharmacy	**1M**
	t.	**Megaloblastic Anaemia is a types of ……..** **Answer:** ii) Macrocytic	**1M**

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