CLINICAL THERAPEUTICS 6: DISEASES OF THE CENTRAL NERVOUS SYSTEM I

PHAB3HG2

Time allowed: 2 hours

Part ONE. Answer ALL questions. Mark the correct answer CLEARLY on the answer grid provided.

Part TWO. Answer THREE (3) of the FOUR (4) questions. Use a SEPARATE answer book for EACH question in Part TWO.

The marks distribution is shown for each section of each question.

The mark allocation for the paper is:
Part ONE carries 40 % of the total mark
Part TWO carries 60 % of the total mark

This paper consists of 12 pages in total.

Notes are not permitted in this examination. Do not take this paper out of the examination room. Do not turn over until you are told to do so by an invigilator.
PART ONE

TYPE 1 MCQs

For each question there is ONE (1) correct answer only.

1. Which ONE of the following is NOT a function of the hypothalamus?
   A) Production of hormones
   B) Regulation of emotions and behaviour
   C) Regulation of eating and drinking
   D) Control of body temperature
   E) Control of motor activity

2. Which ONE of the following is the broad band of white matter that connects the left and right cerebral hemispheres?
   A) Hypothalamus
   B) Basal nucleii
   C) Lateral ventricle
   D) Corpus callosum
   E) Diencephalon

3. Which ONE of the following statements is INCORRECT regarding transmission at the glutaminergic synapse?
   A) Glutamate action is terminated by enzymatic breakdown in the synaptic cleft
   B) Glutamate is synthesised from glutamine by the enzyme glutaminase
   C) Glutamate transporters are present on the cell membrane of surrounding astrocytes
   D) Glutamate receptors can be either ionotropic or metabotropic
   E) Glutamate is an excitatory neurotransmitter

4. GABA_\text{A} receptors are which ONE of the following?
   A) Ligand-gated Cl\textsuperscript{\textsuperscript{\textsuperscript{-}}} channels
   B) G protein-coupled receptors
   C) Ligand-gated cation channels
   D) Nuclear receptors
   E) Tyrosine kinase-coupled receptors
5. Which **ONE** of the following is the major signalling pathway for $\alpha_1$-adrenoceptors?

A) Activation of phospholipase C and generation of inositol trisphosphate
B) Inhibition of adenylate cyclase and subsequent cAMP production
C) Inhibition of phospholipase C and generation of inositol trisphosphate
D) Decreased intracellular calcium
E) Activation of adenylate cyclase and subsequent cAMP production

6. According to the UK PDS Brain Bank criteria, which **ONE** of the following is an exclusion criterion for Parkinson's disease?

A) Muscular rigidity
B) Use of anti-psychotic medication
C) Rest tremor
D) Excellent response to levodopa
E) Unilateral onset

7. Which **ONE** of the following drugs is a dopa-decarboxylase inhibitor?

A) Levodopa
B) Entacapone
C) Selegiline
D) Apomorphine
E) Carbidopa

8. Which **ONE** of the following statements is **CORRECT** in explaining why a dopa-decarboxylase inhibitor must always be combined with levodopa?

A) It inhibits the breakdown of levodopa in the brain
B) It facilitates the breakdown of levodopa in the periphery
C) It facilitates the absorption of levodopa from the gastrointestinal tract
D) It facilitates the breakdown of levodopa in the brain
E) It inhibits the breakdown of levodopa in the periphery

9. Extracellular deposits of $\beta$-amyloid protein and interneuronal tangles of tau protein are characteristic of which **ONE** of the following conditions?

A) Parkinson's Disease
B) Motor Neurone Disease
C) Alzheimer's Disease
D) Huntington's Disease
E) New variant CJD

**TURN OVER**
10. Which **ONE** of the following drugs used to treat Alzheimer’s disease is an NMDA receptor antagonist?

A) Donepezil  
B) Memantine  
C) Rivastigmine  
D) Gallantamine  
E) Ginkgo biloba

11. The orphan receptor has which **ONE** of the following as a natural ligand?

A) Enkephalin  
B) Dynorphin  
C) Endorphin  
D) Endomorphin  
E) Nociceptin

12. Which **ONE** set of interactions is important in the binding of enkephalins according to the Portoghese theory?

A) Tyrosine OH, negative charge on carboxyl terminus and van der Waals interactions from a glycine  
B) Tyrosine OH, positive charge on the amino terminus and van der Waals interactions from isoleucine  
C) Phenylalanine aromatic residue, tyrosine OH and positive charge on the amino terminus  
D) Phenylalanine aromatic residue, tyrosine OH and van der Waals interactions from glycine  
E) Negative charge on the carboxyl terminus, tyrosine OH and van der Waals interactions from isoleucine

13. Binding at the kappa receptor results in **TWO** of the following effects:

i) Analgesia  
ii) Respiratory depression  
iii) Sedation  
iv) Euphoria  
v) Addiction

Which **ONE** of the following are the **TWO** effects that are observed?

A) ii and iv  
B) i and iii  
C) i and ii  
D) i and iv  
E) iii and v
14. Which **ONE** of the following receptors does morphine binds most strongly to?

A) The delta ($\delta$) receptor  
B) The orphan receptor  
C) The sigma ($\sigma$) receptor  
D) The mu ($\mu$) receptor  
E) The kappa ($\kappa$) receptor

15. Which **ONE** of the following patients would be classified as a ‘migraineur’ according to the International Headache Society (IHS) classification?

A) A patient with four attacks of headaches, lasting for 24 hours that throb and are aggravated by movement. They also suffer from a dislike of bright lights and noise during the attack but no other symptoms  
B) A patient with six attacks of headaches, lasting 36 hours that start on one side of the head, throb and are severe in intensity. They have no other symptoms  
C) A patient with eight attacks of headaches, lasting 86 hours that are aggravated by activity and severe in intensity. They also suffer from nausea and vomiting during the attack, but no other symptoms  
D) A patient with ten attacks of headaches, lasting 48 hours that are moderate severity. They also suffer from vomiting and photophobia during the attack, but no other symptoms  
E) A patient with twelve attacks of headaches lasting 72 hours, on one side of the head and throbbing. They also suffer from nausea and vomiting during the attack, but no other symptoms

16. Which **ONE** of the following would be the **MOST** appropriate medication for a migraine sufferer who has very intense quick onset headaches during the start of the attack, together with lots of nausea and vomiting?

A) Naratriptan tablets  
B) Eletriptan tablets  
C) Co-codamol tablets  
D) Sumatriptan nasal spray  
E) Zolmitriptan orodispersable tablets

17. Which **ONE** of the following anti-emetic drugs does **NOT** work by directly antagonising the action of a neurotransmitter?

A) Metoclopramide  
B) Ondansetron  
C) Hyoscine  
D) Cinnarazine  
E) Nabilone
18. **Which ONE of the following is the type of pain associated with injury to the peripheral and/or central nervous system?**

A) Visceral  
B) Somatic  
C) Neuropathic  
D) Sympathetically maintained  
E) Anginal

19. **According to NICE, which ONE of the following drugs would be first line in the treatment of osteoarthritis for a patient with a high risk of a duodenal ulcer and a low cardiovascular risk?**

A) Ibuprofen  
B) Paracetamol  
C) Celecoxib  
D) Diclofenac  
E) Naproxen

20. **Evidence suggests that topical NSAIDs are only effective for which ONE of the following time periods?**

A) One week  
B) Two weeks  
C) Four weeks  
D) Three months  
E) Six months

21. **Which ONE of the following is NOT characteristic of primary dysmenorrhoea?**

A) Most commonly affects women over 30 years  
B) Pain in absence of pelvic disease  
C) Cramping pain in lower abdomen  
D) Pain starts shortly before menses and usually subsides within 1-2 days of menses  
E) Mild symptoms can be treated OTC
22. In palliative care, which ONE of the following would be the correct first course of action for a patient receiving morphine sulphate modified release tablets (MST) 30mg BD, if they are starting to complain of pain during the middle of the day?

A) Continue with the MST at the same dose and add in a fentanyl patch
B) Stop the MST and put the patient on a subcutaneous infusion of diamorphine
C) Change the dose of MST to 20mg QDS
D) Prescribe an immediate release formulation of morphine to be used PRN in conjunction with the MST, and monitor its use
E) Stop the MST and prescribe an immediate release morphine formulation to be used PRN

23. Carbonic anhydrase inhibitors act to lower intraocular pressure by which ONE of the following mechanisms?

A) Increasing outflow via the trabecular meshwork
B) Causing pupil dilation
C) Increasing outflow via the uveoscleral pathway
D) Causing constriction of the ciliary muscle
E) Decreasing secretion of aqueous humour

24. Which ONE of the following is an example of an inhaled hypnotic used in general anaesthesia?

A) Propofol
B) Thiopentone
C) Etomidate
D) Ketamine
E) Halothane

END OF TYPE 1 MCQs
TYPE 2 MCQ's

Decide which of the responses to the following questions is (are) correct: Then choose:

A) If i, ii and iii are correct  
B) If i and ii only are correct  
C) If ii and iii only are correct  
D) If i only is correct  
E) If iii only is correct

25. Ms DS is a patient of yours, who lives alone and who suffers from migraines. She has been taking paracetamol tablets (1g QDS) and doesn't want to take any other medication but would like to know if there is anything else she could do to improve the management of her migraines. Which of the following would be appropriate advice?

   i) Increase the dose of paracetamol  
   ii) Change to soluble paracetamol  
   iii) Keep a diary to help identify trigger factors

26. MDS has no other medical conditions and decides she would like to try some other medication to help with her migraine. Which of the following would be appropriate next steps in the management of her migraine?

   i) Keep on paracetamol and add ibuprofen (400mg TDS)  
   ii) Stop the paracetamol and start ibuprofen (400mg TDS)  
   iii) Stop the paracetamol and start Co-codamol tablets (8/500mg)

27. A few months later DS returns with a prescription for sumatriptan 50mg tablets. Which of the following would be appropriate counselling for this new medication?

   i) Take the sumatriptan tablets as soon as you feel a headache coming on  
   ii) Don’t take any other medication for migraines, only use the sumatriptan when you have got severe migraine pain  
   iii) Take one sumatriptan tablet and if the pain goes away and then returns you can take a second dose after two hours

28. Which of the following are known potential targets for future migraine specific treatments?

   i) Calcitonin gene-related peptide (CGRP) antagonists  
   ii) 5-HT1D/1F receptor agonists  
   iii) Nitric oxide receptor agonists

END OF TYPE 2 MCQs
TYPE 3 MCQs

Directions:
The following questions consist of a statement in the left-hand column followed by a second statement in the right-hand column.

Decide whether the first statement is TRUE or FALSE.
Decide whether the second statement is TRUE or FALSE.

Then choose:

A) If both statements are TRUE and the second statement is a correct explanation of the first statement
B) If both statements are TRUE but the second statement is NOT a correct explanation of the first statement
C) If the first statement is TRUE but the second statement is FALSE
D) If the first statement is FALSE but the second statement is TRUE
E) If both statements are FALSE

29. FIRST STATEMENT

COX-2 inhibitors should not be prescribed in patients with a history of cardiovascular disease.

SECOND STATEMENT

COX-2 inhibitors selectively inhibit the COX-2 enzyme and thus inhibit platelet aggregation.

30. FIRST STATEMENT

Prostaglandin agonists stimulate the drainage of aqueous humour from the eye via the trabecular meshwork and Schlemm’s canal.

SECOND STATEMENT

In the treatment of glaucoma, prostaglandin agonists are used to reduce intraocular pressure, which is the major risk factor for glaucoma.

END OF PART ONE

TURN OVER
PART TWO

31. Answer **ALL** parts: (a), (b) and (c).

You are a basic grade hospital pharmacist on your rotation of the older people wards. You encounter Mrs JH who has a diagnosis of early Parkinson's disease and your tutor asks you to prepare a case study of this patient for the pharmacy team. Mrs JH is 77 years old and currently prescribed the lowest available dose of levodopa, her prescription is as follows:

Co-beneldopa 12/50mg caps 1 TDS

(Co-beneldopa contains benserazide 12.5mg and levodopa 50mg)

Your tutor has requested that you include answers to the following questions in your presentation.

a) Describe the neurochemical changes associated with Parkinson's disease and the resulting clinical features.  

[30%]

b) Describe the signs and symptoms of the early stages and the later stages of Parkinson's disease.  

[30%]

c) Mrs JH was admitted due to a fall and on examination has dyskinesias. She reports that she feels that her symptoms are not currently being well controlled by her co-beneldopa as the rigidity tends to come back within two hours of taking the co-beneldopa capsule. With reference to NICE guidelines, describe appropriate changes to Mrs JH's therapy to maximize control of her Parkinson's disease. Describe your reason(s) for the change(s) and any risks of adverse effects associated with the change(s).  

[40%]
32. Answer BOTH parts: (a) and (b).
   a) What is excitotoxicity? [10%]
   b) Describe the mechanisms involved in mediation of excitotoxicity. [90%]

33. Answer ALL parts: (a), (b), (c) and (d).

   Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used medicines in the treatment of pain and inflammation.

   a) Discuss their mechanisms of action and how this relates to their therapeutic use. [40%]
   b) Discuss whether COX-2 inhibitors have any advantages or disadvantages in terms of efficacy and safety over traditional NSAIDs. [30%]
   c) Discuss why NICE recommend the use of paracetamol before NSAIDs for the relief of osteoarthritis. [20%]
   d) What other non-drug methods can be recommended for pain relief in osteoarthritis. [10%]
34. Answer **ALL** parts: (a), (b), (c) and (d).

a) Molecules 1 and 2 are both able to act at opioid receptors. Explain the basis of the Snyder theory for binding at opioid receptors and discuss, with the aid of diagrams, which molecule is likely to have antagonist effects [30%]

b) Molecules 3 and 4 are useful in the treatment of constipation but not in the treatment of opioid overdose. Identify and discuss the structural features which account for these properties. [20%]

c) Discuss how and why opiates are used in palliative care, with examples of opiates administered via the oral, subcutaneous and transdermal routes. [30%]

d) What are the main problems with using opiates, and how can these be ameliorated? [20%]

**END OF PAPER**