UNIVERSITI SAINS MALAYSIA

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PROGRAM SARJANA FARMASI
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FCP 555: PHARMACOTHERAPEUTIC IV

(2 HOURS)

This examination consists of **two sections.**

Section A consists of 50 multiple choice questions

Section B consists of **two (2)** long questions

Answer **ALL** questions

Answer to section A must be entered into the scripts provided.

... 2/-

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SECTION A

1. Which of the following statement regarding the use of mannitol in increased intracranial pressure (ICP) is true?

   ..... (a) It should be given parenterally.

   ..... (b) The use should not be longer than 3 days.

   ..... (c) It may induce osmotic diuresis.

   ..... (d) All of the above are true.

2. The use of high dose pentobarbitone in the management of ICP is/are .....

   ..... (a) indicated in vasogenic ICP.

   ..... (b) indicated in obstructive ICP.

   ..... (c) the first line management of ICP related to generalised edema.

   ..... (d) all of the above.

3. The use of corticosteroids in the management of ICP is/are..

   ..... (a) related to its ability to reduce cerebrospinal fluid (CSF) production.

   ..... (b) related to its ability to reduce the leakiness of blood brain barrier.

   ..... (c) related to its ability to shift oxygen dissociation curve.

   ..... (d) all of the above.

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4. Mechanism of action of diuretics in reducing ICP is .....

..... (a) by reducing total body water.

..... (b) by decreasing CSF production.

..... (c) by improving CSF flow.

..... (d) by decreasing the rate of the brain metabolism.

5. The use of hyperosmolar agents in the management of ICP is/are..

..... (a) associated with the reduction of total body water.

..... (b) associated with an increase in the serum osmolarity.

..... (c) very useful in the ICP associated with the presence of mass lession.

..... (d) all of the above.

6. Normal intracranial pressure is .....

..... (a) 15 torr.

..... (b) 15 mm Hg.

..... (c) 15 mm H_2O.

..... (d) none of the above.

7. Prolonged use of mannitol is/are not encouraged due to.....

..... (a) severe rebound phenomenon.

..... (b) reduction in its effectiveness.

..... (c) severe hyperosmolar coma.

..... (d) all of the above

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8. Which of the following statements regarding hypothermia in ICP is true?

..... (a) It is useful in controlling ICP in children not responding to mannitol.

..... (b) It reduces the ICP by regulating the rate of respiration.

..... (c) Reduction of body temperature down below 32°C is always associated with arrhythmias.

..... (d) All of the above are true.

9. Which of the following statements is true regarding combination therapy in ICP?

..... (a) Combination of mannitol and frusemide is the first line pharmacologic therapy.

..... (b) Combination of hypothermia and barbiturate is associated with tachycardia.

..... (C) Combination of cortisosteroid and barbiturate is recommended in vasogenic ICP

..... (D) All of the above.

10. Which of the following is/are the best non-drug therapy in ICP secondary to head injury?

..... (a) Hyperventilation.

..... (b) Elevation of head by 30°.

..... (c) Reduction in fluid supplement.

..... (d) All of the above are true.

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11. Which of the following drugs is the most effective in the management of migraine ?

..... (a) Ergotamine.

..... (b) Propranolol.

..... (c) Mefenamic acid.

..... (d) Carbamazepine.

12. Which of the following statement regarding migraine is true?

..... (a) Aura usually occurs 24 hours prior to an attack.

..... (b) Pulsatile pain is due to vasodilation.

..... (c) The use of cinnarizine is very effective in preventing classical migraine.

..... (d) All of the above are true.

13. Which of the following analgesic is the best choice for migraine attack ?

..... (a) Aspirin.

..... (b) Paracetamol.

..... (c) Piroxicam.

..... (d) Diclofenac Sodium.

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14. Which of the following non-drug therapy is/are effective in reducing the duration of migraine attack?

..... (a) Regular exercise.

..... (b) Avoidance of mental tension.

..... (c) Stay in the dark room and sleep.

..... (d) All of the above.

15. Which of the following statements regarding migraine is true?

..... (a) Prophylaxis therapy is indicated in patient with 2 or more attacks per year.

..... (b) Beta-blockers is the most effective drug for the prophylaxis of classical migraine.

..... (c) Cinnarizine act by preventing vasodilation prior to an attack.

..... (d) All of the above are true.

16. Which of the following sequence regarding the choice of ICP therapy is true ?

..... (a) Mannitol > corticosteroid > phenobarbitone.

..... (b) Mannitol > phenobarbitone > corticosteroid.

..... (c) Corticosteroid > mannitol > phenobarbitone.

..... (d) Phenobarbitone > mannitol > corticosteroid.

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17. Which of the following statement regarding the pathophysiology of migraine is true?

..... (a) Migraine is a manifestation of sequence of vasoconstriction and vasodilation of the extra and intracranial arteries.

..... (b) Platelet aggregation is the main cause of classical migraine.

..... (c) Migraine that occurs after an episode of stress is due to increased ICP

..... (d) All of the above are true.

18. Postural hypotension is commonly known to occur in a psychiatric patient treated with the following antipsychotic drugs except...

..... (a) Chlorpromazine.

..... (b) Thioridazine.

..... (c) Clozapine.

..... (d) Thiothixene.

19. Which of the following mechanism of action of the anti-psychotic drugs is true for lithium carbonate ?

..... (a) It blocks the D1 and D2 receptors.

..... (b) It inhibits the reuptake processes.

..... (c) It inteferes with the storage of neurotransmitter and sodium-potassium pump.

..... (d) It mimics the neurotransmitter at the storage and receptor site.

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20. The following statements concerning the principles of neuroleptic use are true except .....

..... (a) neuroleptics are target symptom specific rather than disease specific.

..... (b) they are not effective in "non-productive" symptoms.

..... (c) there is a significant difference between the neuroleptics in their effectiveness.

..... (d) the dose of neuroleptic should be reduced to the least possible dose once psychosis is controlled.

21. The abnormality in Parkinson's disease is due to the .....

..... (a) degeneration of the lateral nucleus of the thalamus.

..... (b) degeneration of the subthalamic nucleus.

..... (c) loss of pallidal neurons.

..... (d) loss of substantia nigra neurons.

22. Which of the following is not a cause of Parkinsonism ?

..... (a) Reserpine treatment.

..... (b) A focal lesion of the brain.

..... (c) Encephalitis Lethargica.

..... (d) Carbon monoxide poisoning.

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23. Which of the following is a therapy for idiopathic Parkinsonism ?

..... (a) Prochlorperazine.

..... (b) Amantadine.

..... (c) Thalamotomy.

..... (d) Prednisolone.

24. The most effective drug in the treatment of Parkinson's disease is .....

..... (a) levodopa.

..... (b) anticholinergic.

..... (c) bromocriptine.

..... (d) monoamine oxidase inhibitors (MAOI).

25. The most common etiology for Parkinsonism is .....

..... (a) tumors.

..... (b) trauma.

..... (c) infection.

..... (d) idiopathic.

26. The type of tremor observed in Parkinsonism is .....

..... (a) intentional tremor.

..... (b) postural tremor.

..... (c) resting tremor.

..... (d) action tremor.

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27. Which of the following drug would interact with levodopa and cause hypertensive crisis ?

..... (a) Phenytoin.

..... (b) Pyridoxine.

..... (c) Methyldopa.

..... (d) MAOI.

28. Which of the following is regarded as typical extrapyramidal disorder ?

..... (a) It disappears during sleep.

..... (b) It is relieved by alcohol.

..... (c) It is not affected by stress.

..... (d) It is characterised by weakness.

29. Which of the following neuroleptic has the highest potential to induce extrapyramidal syndrome (EPS) ?

..... (a) Fluphenazine.

..... (b) Chlorpromazine.

..... (c) Perphenazine.

..... (d) Mesoridazine.

30. Acute dystonia symptoms usually affect the .....

.....(a) head and neck area of the body.

.....(b) upper limbs.

.....(c) lower limbs.

.....(d) middle portion of the body.

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31. Anticholinergics is not employed in the treatment of.....

.....(a) acute dystonia.

.....(b) akathisia.

.....(c) pseudoparkinsonism.

.....(d) tardive dyskinesia.

32. Which of the following EPS is characterised by internal motor restlessness ?

..... (a) Akathisia.

..... (b) Dystonia.

..... (c) Pseudoparkinsonism.

..... (d) Tardive dyskinesia.

33. The antibody involved in the destruction of the post-junctional end-plate acetylcholine receptors in myaesthenia gravis is the ..... type.

..... (a) IgG.

..... (b) IgM.

..... (c) IgE.

..... (d) all of the above.

34. Which of the following anticholinesterase is being employed in the comfirmatory test of myaesthenia gravis ?

..... (a) Edrophonium chloride.

..... (b) Ambenonium chloride.

..... (c) Pyridostigmine bromide.

..... (d) Neostigmine bromide.

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35. Which of the following anticholinesterase has the longest duration of action ?

..... (a) Edrophonium chloride.

..... (b) Ambenonium chloride.

..... (c) Pyridostigmine bromide.

..... (d) Neostigmine bromide.

36. The main cause of death in myaesthenia gravis patients is.....

..... (a) cardiovascular problems.

..... (b) liver dysfunction.

..... (c) renal failure.

..... (d) respiratory weakness.

37. The reason that hospitalization is recommended when a myaesthenia gravis patient is to be started on corticosteroid is.....

..... (a) the initiation dose is very high.

..... (b) it is usual for patients above 60 years of age.

..... (c) it augments muscle weakness initially.

..... (d) it usually causes severe hypertension.

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38. Optimal dose of anticholinesterase would only be able to restore the muscle strength to ..... of the normal strength.

.....(a) 20 percent.

.....(b) 40 percent.

.....(c) 60 percent.

.....(d) 80 percent.

39. The following is a type of hallucination except .....

..... (a) visual.

..... (b) somatic.

..... (c) persecutory.

..... (d) tactile.

40. Characteristic features of schizophrenia is .....

..... (a) flight of idea.

..... (b) elation.

..... (c) delusion.

..... (d) concrete thinking.

41. Antipsychotic drug which has the most anticholinergic side-effect is .....

..... (a) thioridazine.

..... (b) trifluoperazine.

..... (c) chlorpromazine

..... (d) perphenazine.

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42. The average daily dose of chloropromazine for treatment of acute psychotic illness is .....

..... (a) 1,000 mg - 1,500 mg.

..... (b) 500 - 1,000 mg.

..... (c) 100 - 300 mg.

..... (d) 400 - 700 mg.

43. Characteristic features of mania is .....

..... (a) pressure of speech.

..... (b) thought block.

..... (c) loosening of association.

..... (d) flight of idea.

44. Which of the following investigation is mandatory before starting lithium therapy ?

..... (a) Liver function test.

..... (b) Serum creatinine.

..... (c) Full blood picture.

..... (d) Serum electrolyte.

45. Tetracyclic anti-depressant available in Hospital USM is ..

..... (a) amitriptyline.

..... (b) Imipramine.

..... (c) Dothiepin.

..... (d) Maprotiline.

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46. Second line drug used in the prophylactic treatment of affective disorder is .....

..... (a) carbamazepine.

..... (b) alprazolam.

..... (c) haloperidol.

..... (d) lithium carbonate

47. Which of the following disorder is classified as neurotic illness ?

..... (a) Paranoid disorder.

..... (b) Neurotic depression.

..... (c) Schizophreniform disorder.

..... (d) Delirium.

48. Characteristic features of depression is .....

..... (a) palpitation.

..... (b) tremors.

..... (c) anorexia.

..... (d) obsessive idea.

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49. Which of the following drug is commonly used in the treatment of anxiety neurosis ?

..... (a) Midazolam.

..... (b) Sodium barbiturate.

..... (c) Clonazepam.

..... (d) Propranolol.

50. Behaviour treatment for anxiety disorder is .....

..... (a) systematic desensitization.

..... (b) token economy.

..... (c) response prevention.

..... (d) aversion therapy.

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SECTION B

Question 1.

Mr. MA is a 37 years old malay man, was referred to HUSM from Jertih Distric Hospital for further management of CVA post-MVA.

Case summary Mr. MA was otherwise healthy until 3 days ago when he was involved in a motor vehicle accident (MVA) while he was riding his motorcycle. During the incident, he sustained a severe head injury with massive blood loss. On admission to the Jertih District hospital, he was found to be unconcious with Glasgow Coma Score of 5. During the first 3 days in the hospital he was given 4 pints of blood and 8 litres of dextrose saline. In addition, he received mannitol and phenytoin but failed to regain conciousness. He was referred to HUSM for further investigation and management.

In HUSM, a CT scan was done and the result showed a large intracerebral hemorrhage surrounded by edema at the frontal lobe. However, there was no sign of persistent bleeding. Various laboratory tests were ordered and the results were still pending.

A. Explain the possible mechanism for the development of increased intracranial pressure in MA ?

(7 marks)

B. Explain the rationale for the use of mannitol in MA. Suggest the monitoring plan to evaluate the effect of mannitol therapy.

(8 marks)

C. Discuss other therapeutic approaches of managing increased intracranial pressure.

(10 marks)

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Question 2.

SM, a 50 year old female complained of anxiety, nervousness, tremor and weakness of the right hand. Her tremor and weakness were first noticed at the time of her husband's death 5 months ago. Her complaints were exacerbated by stress and worsened by pressure at work. Her secretary told her that her handwriting is getting smaller and irregular and her voice is changing.

Physical examination	: well nourished
	: well developed
	: no acute distress
	: noticeable tremor in both hands
	: cogwheel rigidity in both arms
	: slightly mask like face
	: sialorrhea
Vital signs	: B.P. 130/90
	: T 37 C
	: R.R 20
Laboratory tests	: all within normal limits.
Diagnosis	: Parkinson's disease
Treatment Plan	: Anticholinergic.

A. What subjective and objective clinical data are compatible with a diagnosis of Parkinson's disease in SM ?

(5 Marks)

B. Suggest an anticholinergic which is suitable for SM and discuss the monitoring parameters that should be done to assess the efficacy and adverse effect of the drug suggested.

(5 Marks)

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C. Five months later her signs and symptoms improved except for her rigidity and bradykinesia which became more troublesome. Levodopa was then added to the prescription. Discuss the suitability of levodopa and how it should be initiated. Also discuss its mechanism of action and adverse drug reactions.

(10 Marks)

(D) Discuss the advantages and disadvantages of using carbidopa in combination with levodopa ?

(5 Marks)

Appendix

Normal Laboratory Values

1.	Ammonia	80-110 mcg/dl or	47-65 umol/L
2.	Amilase	4-25 IU/ml	
3.	Billirubin		
	- Direct	0-0.2 mg/gl	0-3 umol/L
	- Indirect	0.2-0.8 mg/dl	30-14 umol/L
	- Total	0.2-1 mg/dl	30-17 umol/L
4.	CO_2	20-30 mEq/L	24-30 mMol/L
5.	pCO_2	35-45 mmHg	
6.	CI	100-106 mEq/L	100-106 mMol/L
7.	Cpk	50-170 U/L	
8.	Creatinine (SCr)	0.6-1.5 mg/dl	60-130 umol/L
9.	Random blood sugar	70-110 mg/dl	3-10 umol/L
10.	Iron	50-150 mcg/dl	9.0-26.9 umol/L
11.	Lactic dehydrogenase	70-210 IU/L	
12.	Magnessium	1.5-2.0 mEq/L	0.8-1.3 mMol/L
13.	pO_2	75-100 mmHg	
14.	pH	7.35-7.45	
15.	Acid phosphatase		
	Male	0.13-0.63 IU/ml	36-176 nmol s^{-1}/L
	Female	0.101-0.65 IU/ml	2.8-156 nmol s^{-1}/L
16.	Alkaline phosphatase	39-117 IU/L	
17.	Phosphorous	3.0-4.5 mg/dl	1.0-1.5 mMol/L
18.	Potassium (K+)	3.5-5.0 mEq/L	3.5-5.0 mMol/L
19.	Calcium (Ca^{2+})	8.5-10.5 mg/dl	2.1-2.6 mMol/L
20.	Sodium (Na+)	135-145 mEq/L	135-145 mMol/L
21.	Bicarbonate (HCO_3-)	24-38 mEq/L	24-28 mMol/L

22.	Protein		
	- Total	6.0-8.5 g/dl	60-85 g/L
	- Albumin	3.5-5.0 g/dl	35-50 g/L
	- Globulin	2.3-3.5 g/dl	23-35 g/L
	- Transferrin	200-400 mg/dl	2.0-9.0 g/L
23.	Transaminase (SGOT)	0-40 IU/L	0-0.32 umol s^{-1}/L
24.	BUN	8-25 mg/dl	2.9-8.9 mMol/L
25.	Uric Acid	3-7 mg/dl	0.18-0.42 mMol/L
26.	Blood Pictures		
	Red blood cell (RBC)		
	Male	4.8-6.4 x $10^6/mm^3$	
	Female	4.2-5.4 x $10^6/mm^3$	
	White blood cell(WBC)	4.0-11.0 x $10^3/mm^3$	
	P	60-75%	
	L	20-40%	
	M	4-8%	
	B	0-1%	
	E	1-3%	
	Platelate (Plt)	200-400 x $10^3/mm^3$	
27.	ESR Male	0-10 mm/jam (Wintrobe)	
	Female	0-15 mm/jam (Wintrobe)	
28.	Hematocrit		
	Male	45-52%	
	Female	37-48%	
29.	Hemoglobine (Hgb)		
	Male	13-18 g/dl	
	Female	12-16 g/dl	
30.	Prothrombin time (PT)	75-100% nilai asas	
31.	APTT	25-37 saat	
32.	Creatinine Clearance (CrCl)	105-150 ml/min/1.73 m^2	
33.	TT_4	3.0-7.5 mcg/dl	
34.	RT_3U	25-35%	
35.	FTI	1.3-4.2	

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NORMAL HEMODYNAMIC VALUES AND DERIVED INDICES

		Normal Value	Units
BP S/D/M	Blood Pressure Systolic/Diastolic/Mean	120/80/93	mm Hg
CO	Cardiac Output	4-6	Liters/min.
RAP	Right Atrial Pressure (Mean)	2-6	mm Hg
PAP S/D/M	Pulmonary Artery Pressure Systolic/Diastolic/Mean	25/12/16	mm Hg
PCWP	Pulmonary Capillary Wedge Pressure (mean)	5-12	mm Hg
CI	Cardiac Index $CI = \frac{CO}{\text{Body Surface Area}}$	2.5-3.5	Liters/min/m^2
SV	Stroke Volume $SV = \frac{CO}{\text{Heat Rate}}$	60 - 80	ml/beat
SVI	Stroke Volume Index $SVI = \frac{SVI}{\text{Body Surface Area}}$	30 - 50	ml/beat/m^2
PVR	Pulmonary Vascular Resistance $PVR = \frac{MPAP - PCWP}{CO} \times 80$	< 200	dynes.sec.cm^{-5}
TPVR	Total Peripheral Vascular Resistance $TPVR = \frac{MBP - RAP}{CO} \times 80$	900-1400	dynes.sec.cm^{-5}
LVSWI	Left Ventricular Stroke Work Index $LVSWI = (MBP-PCWP)(SVI)(.0136)$	35-80	gm-m/m^2/beat