UNIVERSITY OF EAST ANGLIA
School of Pharmacy
Main series UG Examination 2015-16

NEUROPHYSIOLOGY, SYNAPTIC PHARMACOLOGY AND ENDOCRINOLOGY

PHA-5004Y

Time allowed: 2 hours

Part ONE

Answer ALL questions. For each question, there is ONE correct answer. Use the answer grid provided for ALL your answers.

Part TWO

This part has a single question. This question is COMPULSARY. Use a SEPARATE answer book for this question.

Part THREE

Answer TWO of the THREE questions. Use a SEPARATE answer book for EACH question in Part THREE.

Each question has the same value.
The marks distribution is shown as a percentage for each section of each question.
Answer ALL parts of each of the individual questions you select.

The mark allocation for the paper is:
• Part ONE carries 40% of the total mark.
• Part TWO carries 20% of the total mark.
• Part THREE carries 40% of the total mark.

You are advised to spend approximately 50 min on Part ONE, 20 min on Part TWO and 50 min on Part THREE.

The paper consists of 12 pages in total.

The following is provided: Multiple choice answer grid.

Dictionaries are not permitted in this examination.

Notes are not permitted in this examination.

Do not take this question paper out of the examinations room.

Do not turn over until you are told to do so by the Invigilator.
PART ONE

SECTION A – TYPE 1 MCQ – Single Best Answer

Answer ALL questions. For each question, there is ONE correct answer. Use the answer grid provided for ALL your answers.

1. Which ONE of the following is the major factor controlling insulin secretion?

(A) Stimulation of the parasympathetic nervous system
(B) Blood leucine concentration
(C) Levels of circulating glucagon
(D) Blood glucose concentration
(E) Stimulation of the sympathetic nervous system

2. Which ONE of the following hormones is NOT involved in fuel metabolism?

(A) Somatostatin
(B) Parathyroid hormone
(C) Glucagon
(D) Insulin
(E) Cortisol

3. Which ONE of the following is NOT a sign or symptom of Hyperosmolar non-ketotic (HONK) syndrome?

(A) Ketone breath
(B) Weakness
(C) Dehydration
(D) Reduced consciousness
(E) Nausea and vomiting

4. Which ONE of the following statements concerning diabetes mellitus (DM) is INCORRECT?

(A) Diabetic ketoacidosis can be caused by acute illness e.g. infection
(B) Insulin administered into the buttocks has the slowest absorption
(C) Type 2 DM accounts for 40% of all cases of DM
(D) Type 1 DM is caused by the formation of autoantibodies against the body’s pancreatic β-cells
(E) Obesity causes an increase in insulin resistance and contributes to the development of Type 2 DM
5. The natural product phlorizin from apple trees has an antidiabetic effect due to inhibition of the sodium-dependent glucose co-transporters (SGLTs). Which ONE of the following is NOT a reason for the use of phlorizin as a drug?

(A) Phlorizin is susceptible to metabolic breakdown by glycoside hydrolysis
(B) Glycoside hydrolysis releases a toxic by-product
(C) Phlorizin is a nonselective inhibitor of SGLT1 and SGLT2 leading to side effects
(D) The aryl side-chains cause an unacceptably high increase in lipophilicity
(E) Its use results in excretion of glucose in the urine

6. Which ONE of the following statements concerning the physico-chemical nature of insulin is INCORRECT?

(A) Bovine insulin rather than porcine insulin is closer in chemical structure to human insulin
(B) Chain A has 21 amino acid residues
(C) There are three disulphide bridges in one molecule of insulin
(D) Chain B has 30 amino acid residues
(E) In the presence of zinc, insulin exists as hexamers

7. Which ONE of the following is a macrovascular complication of diabetes mellitus?

(A) Retinopathy
(B) Coronary heart disease
(C) Diabetic foot ulcer
(D) Erectile dysfunction
(E) Nephropathy
8. Which **ONE** of the following is a contraindication to the use of metformin therapy?

(A) Stroke  
(B) Renal failure  
(C) Hypertension  
(D) Hypothyroidism  
(E) Polycystic ovary syndrome

9. Which **ONE** of the following occurs as a result of an increase in circulating insulin levels?

(A) Increased glycogenolysis  
(B) Increased lipolysis  
(C) Increased gluconeogenesis  
(D) Increased uptake of amino acids into cells  
(E) Increased absorption of glucose from the small intestine

10. Insulin mediates its cellular actions by which **ONE** of the following types of receptor?

(A) A glucose transporter  
(B) A G protein-coupled receptor  
(C) A ligand-gated ion channel  
(D) A tyrosine kinase-coupled receptor  
(E) A nuclear receptor

11. Which **ONE** of the following is **NOT** a World Health Organisation (WHO) diagnostic criterion of diabetes mellitus?

(A) Polyuria and polydipsia  
(B) Random venous plasma glucose of > 11.1 mmol / L  
(C) Fasting venous plasma glucose of < 7.0 mmol / L  
(D) Plasma glucose of > 11.1 mmol / L two hours after an oral glucose tolerance test  
(E) Fasting venous plasma glucose of > 7.0 mmol / L
12. With respect to the monitoring of diabetes mellitus (DM) which ONE of the following statements is INCORRECT?

(A) People with type 2 DM should have their kidney function and blood lipid levels monitored
(B) According to NICE the target HbA1c for a patient with diabetes is less than 6.5 to 7.5 % (48-58 mmol/mol)
(C) The target blood pressure for someone with diabetes and retinopathy is <130/80
(D) Patients with diabetes should have their urine checked for the presence of microalbuminuria
(E) Patients with diabetes should have their eyes checked for retinopathy every 5 years

13. Which of the following statements regarding drug use in pregnancy is INCORRECT?

(A) The foetus is most at risk of adverse effects of drugs between 3 and 8 weeks gestation
(B) Approximately 20-25% of all birth defects result from drug use in pregnancy
(C) Thalidomide should not be used during pregnancy due to the risk of limb malformation in the foetus
(D) Drugs which are more likely to cross the placenta are unionised and lipophilic
(E) 90% of women take drugs at some point during pregnancy

14. A patient receiving carbimazole for hyperthyroidism visits your pharmacy with a sore throat and asks for your advice. Which is the most appropriate recommendation?

(A) Paracetamol
(B) Nothing at present but return in one week if still has symptoms
(C) Strepsils® sore throat lozenges
(D) Immediate referral to GP
(E) Menthol and eucalyptus inhalation

15. Which ONE of the following statements is CORRECT? The blood test results that will be seen in a patient who has been diagnosed with hypothyroidism are:

(A) Low TSH, Low T4, Low T3
(B) High TSH, High T4, High T3
(C) High TSH, Low T4, Low T3
(D) Low TSH, High T4, High T3
(E) High TSH, Low T4, High T3
16. Which **ONE** of the following is **NOT** a sign or symptom of Cushing’s Syndrome?

(A) Glucose intolerance  
(B) Hyperpigmentation of skin  
(C) “Moon” face  
(D) Psychosis  
(E) Hirsutism

17. Which **ONE** of the following is **NOT** an adverse effect of corticosteroid therapy?

(A) Hypertension  
(B) Osteoporosis  
(C) Growth suppression in children  
(D) Anorexia  
(E) Immunosuppression

18. Absence of the 21-hydroxylase enzyme results in which **ONE** of the following?

(A) An increase in corticosteroid and mineralocorticoid production  
(B) A decrease in corticosteroid and increase in mineralocorticoid production  
(C) A decrease in corticosteroid and no change in mineralocorticoid production  
(D) An increase in corticosteroid and no change in mineralocorticoid production  
(E) A decrease in corticosteroid and mineralocorticoid production

19. With respect to the female menstrual cycle which **ONE** of the following is **INCORRECT**?

(A) During the follicular phase the dominant follicle grows in size  
(B) At ovulation the pituitary gland produces high levels of FSH and LH  
(C) If fertilisation occurs during the luteal phase the implanted embryo secretes human chorionic gonadotrophin (hCG) which is detected during a pregnancy test  
(D) Cervical mucus is at its thickest at ovulation  
(E) Oestrogen levels are at their highest at the end of the follicular phase

20. Which **ONE** of the following is **NOT** a sign or symptom of female hypogonadism?

(A) Hirsutism  
(B) Subfertility  
(C) Amenorrhoea  
(D) Dry vagina  
(E) Poor libido
SEtion B – Type 2 MCQ – extended matching

The following list of options applies to questions 21-23.

Men’s Health

(A) Alprostadil injections
(B) Finasteride tablets
(C) Minoxidil tablets
(D) Sildenafil tablets
(E) Tamsulosin capsules
(F) Transurethral Incision of the Prostate (TUIP)
(G) Transurethral Resection of the Prostate (TURP)
(H) Watchful waiting

For the patients described, select the most suitable treatment from the list above. Each option may be used once, more than once, or not at all.

21. A 62 year old male with erectile dysfunction for whom tadalafil is contraindicated because of his unstable angina.

22. A 55 year old male has an International Prostate Symptom Score of 3 and no other symptoms.

23. A 73 year old male has an International Prostate Symptom Score of 12 and a prostate estimated to be larger than 30g.
The following list of options applies to questions 24-26.

**Osteoporosis**

(A) Alendronic acid  
(B) Prednisolone  
(C) Calcichew D₃ Forte®  
(D) Calcitonin  
(E) Strontium  
(F) Zolendronic acid  
(G) Raloxifene  
(H) HRT

For each of the following statements, select the best option from the list above. Each option may be used once, more than once, or not at all.

24. Should be taken 30 minutes before breakfast in an upright position and remain upright for 30 minutes after.

25. Administered by injection once every year and acts by absorbing on to hydroxyapatite crystals in the bone.

26. First line agent used in the prevention of steroid induced osteoporosis.
The following list of options applies to questions 27-30.

Complications of diabetes mellitus (DM)

(A) Amitriptyline  
(B) Atenolol  
(C) Atorvastatin  
(D) Gliclazide  
(E) Human Actrapid® sliding scale  
(F) Metformin  
(G) Ramipril  
(H) Salicylic acid

For the complications of DM described, select the most suitable treatment from the list above. Each option may be used once, more than once, or not at all.

27. Prevention of diabetic nephropathy and control of blood pressure.


29. To provide good blood glucose control and prevention of macrovascular complications.

30. For pain control in diabetic neuropathy.

END OF PART ONE
PART TWO

This part has a single question. Use a SEPARATE answer book for this question.

31. Answer ALL parts.

(a) What are the signs and symptoms of hyperthyroidism? [20%]

(b) What is the mechanism by which there is an increase in sympathetic nervous system-mediated signs/symptoms? [20%]

(c) Discuss the rationale for using a β-blocker in the treatment of hyperthyroidism. With reference to the mechanism of action, predict which signs/symptoms would be controlled by a β-blocker. [60%]

END OF PART TWO
PART THREE

Answer TWO of the THREE questions. Use a SEPARATE answer book for EACH question.

32. Answer ALL parts (a) to (c).

(a) As part of an investigation developing novel oestrogen antagonists you synthesise analogue 1 using clomiphene as a lead compound.

\[
\begin{align*}
\text{Clomiphene} & \quad \text{Analogue 1} \\
\text{O} & \quad \text{NMe}_2 \quad \text{O} \\
\quad \text{Cl} & \quad \text{F}
\end{align*}
\]

Fully explain two errors that have been made in the design of the structure of this analogue. [40%]

(b) Describe the actions and effects on the female of the following sex hormones:

(i) Oestrogen

(ii) Progesterone [30%]

(c) Describe the advantages and disadvantages of the following forms of non-hormonal contraception:

(i) Intrauterine device (IUD)

(ii) Diaphragm/cap

(iii) Male condom [30%]
33. Answer ALL parts (a) to (c).

(a) Ideal insulin replacement therapy for diabetic patients should be able to mimic natural physiological insulin needs. In order to achieve this, intermediate-acting and long-acting injectable insulin products have been developed and are often used in combination with rapid-acting insulin. An example is Insuman® Comb 15, a biphasic isophane insulin suspension consisting of 15% dissolved soluble insulin and 85% crystalline protamine insulin. The patient should inject the product 20-30 minutes before breakfast and 20-30 minutes before their evening meal.

Draw a diagram to illustrate the pharmacokinetics (PK) of this product and explain the physicochemical reason behind the manner of its PK action. [40%]

(b) Give an example of a long-acting human insulin analogue and describe its key physicochemical properties. [10%]

(c) Describe the clinical manifestations of early or undiagnosed diabetes mellitus (DM). Your answer should identify those that are different in Type 1 DM and Type 2 DM and those that are common to both. [50%]

34. Answer ALL parts (a) to (c).

(a) Regarding the pituitary gland, name and describe the physiological actions of TWO anterior pituitary hormones. [30%]

(b) Regarding the pituitary gland, name and describe the physiological actions of TWO posterior pituitary hormones. [30%]

(c) Describe the benefits and risks of using hormone replacement therapy (HRT). Outline the difference between oestrogen only and combined preparations, giving details of when each should be used. [40%]

END OF PAPER
School of Pharmacy

Examination Feedback Summary

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<th>Module Name</th>
<th>Clinical Therapeutics 1: Neurophysiology, Synaptic Pharmacology and Endocrinology</th>
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MCQ (Questions 1 to 30):

Mean mark: 62% Max. mark: 90% Min. mark: 30%

Comments: Performance generally good. No individual questions were identified as being a particularly problem. No specific subject areas identified as a particular problem.

Question: 31
(Compulsory)

No. of attempts 94

Comments:

This question integrated knowledge and understanding from both semester 1 (Neuropharmacology) and semester 2 (Endocrinology). Part (a) asked for signs and symptoms of hyperthyroidism and part (b) asked for the mechanism by which sympathetic signs/symptoms were mediated. Most gave some signs/symptoms, although it is notable that these were generally limited in number – when asked such a question it is advisable to list as many as possible. Part (b) was not well answered, with few understanding that T3 leads to an increased expression of beta-receptors. Part (c) asked which signs/symptoms would be predicted to be controlled by a beta-blocker. This gave the opportunity to take each sign/symptom in turn and give reasons whether or not they were mediated by beta-receptors and therefore whether a beta-blocker would be effective. There were some very good answers given, with clear ability to apply neuropharmacological concepts. Most answers discussed tachycardia well. However, fewer answers discussed other signs/symptoms that they had listed.

Question: 32

No. of attempts 58

Comments:

Overall students performed well in this question. Part (a) was extremely well answered with most students demonstrating they had grasped the concepts (far superior answers to previous years potentially demonstrating advantage of TBL as a form of teaching!). In part (b) on actions and effects of oestrogen and progesterone, students who received lower marks did so due to lack of detail or confusing the two hormones. Part (c) on non-hormonal contraceptives was well answered by most students. The question was worth 30% of the marks and students were expected to give 10 points detailing advantages or disadvantages of each to obtain maximum marks.

Question: 33

No. of attempts 61

Comments:

This was the weakest of the 3 questions in part 3. For part (a) most students explained briefly the rationale of taking the injection before breakfast and dinner. However, the drawings of the diagram of PK of a combined administration of intermediate/long-acting with rapid-acting insulin were not fully accurate. The diagram should have rapid onset followed by prolong basal insulin activity over 12 hours. Most students did not label the diagram properly. About half of the students explained the physicochemical properties of the product (such as the difference between crystalline protamine, dissolved and isophane insulin). Most students answered part (b) well with a correct example and the key physicochemical properties were explained. Part (c) was worth 50% of the marks for the question and students were expected to include...
details of common symptoms, those for Type 1 (e.g. DKA), Type 2 (e.g. infections/HONK) and the potential for complications being the first presenting clinical manifestation. Students who received lower marks were those who did not differentiate between clinical manifestations of Type 1 and Type 2 diabetes and those who lacked detail.

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<th>No. of attempts 69</th>
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<td>This question was answered well by most students. Those who received lower marks did so as a result of getting anterior and posterior glands and their hormones in parts (a) and (b) the wrong way round and stating and giving details about cortisol as a hormone produced by the anterior gland which it is not. Students who gained lower marks in part (c) did so due to incorrectly providing details about COC instead of HRT as required by the question.</td>
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