THE COLLEGES OF MEDICINE OF SOUTH AFRICA

Incorporated Association not for gain
Reg No 1955/000003/08

Part I Examination for the Fellowship of the College of Clinical Pharmacologists of South Africa

28 June 2018

Paper 1 (3 hours)

All questions are to be answered. Each question to be answered in a separate book (or books if more than one is required for the one answer)

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1 Discuss the role of protein binding displacement in drug-drug interactions. [10]

2 A 23-year old 28-week pregnant female patient presents with a positive syphilis serologic test and RPR titre 1:16 during antenatal follow-up. She reports a rash and feeling unwell soon after receiving a penicillin injection 2 years ago at the clinic as part of syndromic management of a sexual transmitted disease. The obstetrician contacts you for advice

a) Describe the different types and clinical presentations of penicillin allergy. (10)
b) Discuss your management of this patient. (5)

[15]

3 Mr HD is a 63-year-old man in the surgery ward who has recently had a laparotomy presents with dyspnoea. He was started on low-molecular weight heparin as prophylaxis for deep vein thrombosis post-operatively. Findings on physical examination are unremarkable. Laboratory testing reveals a platelet count of 86 x 10^9/L as compared with 225 x10^9/L at the time of surgery nine days earlier. The results of chest radiography are unremarkable but spiral computed tomography of the chest shows a pulmonary embolism

a) What is the most likely diagnosis? (1)
b) Name 1 risk factor for this diagnosis in this patient. (1)
c) What are the clinical features supporting this diagnosis? (4)
d) Discuss the management of this patient. (5)

[11]

4 a) Write short notes on the receptor regulation theory and provide examples. (6)
b) List and describe 3 non-receptor drug targets and provide an example of each mechanism. (6)

[12]

5 Explain (with examples) the following types of drug agonism

a) Summation agonism. (2)
b) Additive agonism. (2)
c) Synergism (supra additive agonism). (2)
d) Inverse agonism. (2)

[8]

6 Discuss 4 mechanisms of pharmacokinetic drug interactions with an example of each. (8)
Give an example of the following pharmacodynamic interactions
a) Herb-drug interaction. (2)
b) Food-drug interaction. (2)
[12]

7 ABC321 is a novel antimalarial compound that clears P. falciparum parasites faster than any other antimalarial available and can overcome all known mechanisms of antimalarial resistance. The therapeutic dose is expected to be approximately 8mg/kg daily for 3 days. Other positive ABC321 characteristics are the low amount of active ingredient required and that it could be formulated as an injectable for the treatment of severe malaria as well as an oral treatment for uncomplicated malaria. However, there is clear relationship between increasing ABC321 doses and elevations in liver biochemistry, particularly AST and ALT. These elevated transaminases were observed at/above a single dose of 75mg in healthy volunteers (n=36 given 5/10/25/50/75/100mg ABC321; 12 given placebo), but not at 10mg in 12 healthy volunteers in the human challenge model (a controlled human malaria infection in a tightly controlled environment, where the level of parasitaemia is closely monitored in healthy volunteers inoculated with a low number of drug-sensitive parasites and who, around 7 days later, receive the drug candidate). Most elevations were CTCAE grade I-III and there was no concomitant rise in bilirubin. The transaminase rises generally occurred 4-6 days after drug exposure, and all reversed with stopping the drug. The sponsor concluded that there is a relationship between ABC321 and elevated hepatic transaminases, which will need careful patient monitoring in Phase II clinical trials, but there is no reason to stop the programme at this stage
a) Briefly outline 2 mechanisms by which a medicine can cause elevated transaminases. (4)
b) What risk mitigation steps would you implement in your design of the Phase 2a ABC321 clinical trial? (8)
[12]

8 Tabulate the scheduling categories of registered medicines in South Africa to describe the differences in how the scheduling governs the use of medicine and provide one example of a medicine in each schedule. [20]

FC Clin Pharm(SA) Part I

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Paper 2 (3 hours)

All questions are to be answered. Each question to be answered in a separate book (or books if more than one is required for the one answer)

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1 A 4-year-old child presents with irritability, fever and neck stiffness and meningitis is suspected

a) What empiric treatment is appropriate? (1)
b) What pharmacokinetic/pharmacodynamic relationship best describe the efficacy of this treatment? (1)
c) List 3 adverse effects of this treatment. (3)

A 74-year-old female presented with insomnia, depressive mood and suicidal thoughts for the past one month. She is known with hypertension and had a previous myocardial infarction. The antidepressants mianserin, citalopram, amitriptyline and venlafaxine are available in your centre

d) Tabulate the mechanism of action and main side effects of these antidepressants. (8)
e) Choose an antidepressant for this patient and provide reasons. (4)

[17]

2 a) In various circumstances obtaining informed consent for participation in research from the individual is not possible because of a mental inability to do so. Discuss how informed consent could be addressed in this scenario by referring to pertinent ethical principles, laws and guidelines. (10)
b) There is often a fine line between fair compensation for participation in research and undue inducements. Discuss this statement with specific reference to vulnerability. Your answer must include the definition of vulnerability and examples and vulnerable populations in South Africa. (10)

[20]

3 Compare the cost-effectiveness analysis (CEA) with cost-utility analysis (CUA) used in pharmaeconomic evaluation. (10)
What is the difference between efficacy and effectiveness? (2)
Define the following

a) Discounting. (2)
b) Quality adjusted life year. (2)
c) Intangible costs. (2)

[18]

4 Discuss the clinical utility of pharmacogenetics testing in using the following examples

a) Abacavir. (5)

b) Efavirenz. (5)

c) Warfarin. (5)

[15]

5 Answer the following questions about evidence-based medicine and biostatistics

a) What is publication bias? (4)

b) What are the consequences of publication bias? (4)

c) How can publication bias be detected in a meta-analysis? (6)

d) Outline strategies to minimise publication bias. (6)

[20]

6 The national pharmacovigilance centre receives a number of reports of developmental delay in children born to mothers taking a particular antidepressant. Describe 2 study designs that could be used to explore whether intrauterine exposure to the antidepressant causes developmental delay. For each design, list advantages and disadvantages. [10]