Cert ID(SA) Phys

THE COLLEGES OF MEDICINE OF SOUTH AFRICA

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Subspeciality Examination for the Certificate in Infectious Diseases of the College of Physicians of South Africa

23 August 2013

1 Paper Only (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) Outline the utility of procalcitonin (PCT) in rational antibiotic prescribing for respiratory tract infections. (5)

b) Discuss the utility of laboratory tests, therapeutic management and infection prevention control measures for *Clostridium difficile* infection. (10)

[15]

2 You are asked to assist with the management of a 37-year-old man who is a poorly controlled type 1 diabetic patient and gives a history of being treated for pulmonary tuberculosis for the past two months. He now presents with progressive respiratory symptoms and a worsening right upper lobe infiltrate. He claims that he is compliant with his drug therapy and his clinic chart confirms no missed visit with clinic-based directly observed therapy. He is HIV seronegative. Sputum sent for Xpert MTB/RIF test shows *Mycobacterium tuberculosis* complex detected; rifampicin resistant

a) Discuss the common respiratory tract infections that occur in patients with diabetes. (8)

b) How do you interpret the Xpert MTB/RIF result? Discuss the limitations of the test. (4)

c) Discuss your approach to the management of this patient. (8)

[20]

3 A 40-year-old man with poorly controlled diabetes presents with rigors and fever, mild heart failure and a murmur consistent with mitral regurgitation. Two sets of blood cultures done on admission and 24 hours later came back positive for *Staphylococcus aureus*.

a) Discuss any additional investigations you would request and the management of this patient. [8]

b) Compare and contrast community acquired and hospital acquired MRSA under the following headings

i) Epidemiology.

ii) Clinical presentation.

iii) Antibiotic sensitivity and potential antibiotic choices of community acquired MRSA and hospital acquired MRSA. [12]

4 A 19-year-old Mozambican is referred from a clinic in Soweto to the Obstetrics Department of a Johannesburg Hospital in April 2013. According to the notes, she is pregnant, in the early stages of labour, her blood pressure is 90/60, temp 39^{o}C, and appeared 'confused and very ill'. A few bruises were noted on her chest wall. No treatment was given prior to the referral.
At the hospital she is noted to be 39 weeks pregnant and in labour. She has not attended antenatal clinic previously. Very little history is available, other than that she visited Maputo 5 weeks prior to onset of illness to visit family and appeared well the morning before her admission. She is resident in a flat in the inner-city area of Johannesburg and is unemployed.
At the hospital, temperature is 39^{o}C, blood pressure is 80/60 and generalised ecchymoses and petechiae are noted. She appears to be in labour and while the cervix is dilated there is no evidence of any discharge. A preliminary diagnosis of intra-uterine sepsis is made and antibiotic therapy with ampicillin**,** gentamicin and metronidazole is commenced. Her Hb is 9gm/ litre, platelets 96 000, AST 50 and ALT 45. She delivered a macerated foetus 6 hours after admission. She dies 18 hours after admission

a) Discuss the differential diagnosis of this patient. (5)
b) Discuss laboratory tests that you would request. (5)
c) Discuss the management of the patient, including infection control on admission and a public health response based on the most likely diagnosis. (5)

[15]

5 You receive a request for assistance from one of the physicians at a local hospital in Durban, who is concerned that there may be an outbreak in the male medical ward. Over the past 2 days, 5 patients developed fever and diarrhoea with blood and mucous in their stool; these symptoms appear unrelated to their primary diagnoses. Further enquiry reveals that a patient was admitted to the same ward 4 days ago complaining of fever, abdominal pain and blood in the stool. An admission blood culture on the latter patient just came up positive for Gram negative bacilli.

a) What is your clinical diagnosis? Name possible causative agents. (3)
b) Describe your approach in establishing if this is a hospital outbreak. What is the most likely mode of transmission here? (6)
c) If this is an outbreak, how do you propose to control such an outbreak? (2)
d) What is your community response to this outbreak? (4)

[15]

6 A 40-year-old HIV infected patient with a CD4 count of 50 cells/ presents with a right hemiparesis. On CT scan of the brain he has a 4x5 cm abscess in the left parietal lobe with ring enhancement. Aspiration of the lesion reveals Gram positive branching bacilli, which stain positive with a modified ZN stain.

a) Discuss the diagnosis and management of this patient. (5)
b) A HIV infected patient presents with nausea, vomiting and focal signs. His CD4 count is 75. On CT brain the patient has a space occupying ring enhancing lesion. What are the most likely causes? (5)
c) A patient failing a first line antiretroviral therapy regimen of stavudine, lamivudine (3TC) and efavirenz has a genotypic resistance test done, see annexure 1. A new regimen of zidovudine, didanosine and lopinavir/ritonavir is commenced, but virological failure is confirmed after 15 months and a repeat resistance tests is done – see annexure 2 (note that the repeat test shows unchanged reverse transcriptase resistance mutations)
    i) Comment on the choice of second line ART. (2)
    ii) Select a third line ART regimen (restricted to antiretrovirals available in South Africa). (3)

[15]

Annexure 1

Resistance Test on failing 1st line ART

Drug Resistance Interpretation: RT

NRTI Resistance Mutations:	**M41L, M184V, L210W, T215Y**
NNRTI Resistance Mutations:	**K103N, V106M**
Other Mutations:	None

Nucleoside RTI		Non-Nucleoside RTI	
lamivudine (3TC)	High-level resistance	**efavirenz (EFV)**	High-level resistance
abacavir (ABC)	High-level resistance	**etravirine (ETR)**	Susceptible
zidovudine (AZT)	High-level resistance	**nevirapine (NVP)**	High-level resistance
stavudine (D4T)	High-level resistance	**rilpivirine (RPV)**	Susceptible
didanosine (DDI)	High-level resistance		
emtricitabine (FTC)	High-level resistance		
tenofovir (TDF)	Intermediate resistance		

RT Comments

NRTI

- M41L usually occurs with T215Y. M41L+T215Y confer high-level resistance to AZT and d4T and intermediate resistance to ddI, ABC, and TDF. However, in viruses with M184VI, resistance to AZT and d4T will be intermediate and resistance to TDF will be low-level.
- M184VI cause high-level resistance to 3TC and FTC and low-level resistance to ddI and ABC. M184VI are not contraindications to continued treatment with 3TC or FTC because these NRTIs increase susceptibility to AZT, TDF, and d4T and are associated with clinically significant decreased HIV-1 replication. In combination with K101E or E138K, M184I synergistically reduces RPV susceptibility.
- L210W contributes resistance to each of the NRTIs except 3TC and FTC. It usually occurs in combination with M41L and T215Y.
- T215Y causes AZT and d4T resistance and reduces susceptibility to ABC, ddI, and TDF particularly in combination with M41L and L210W.

NNRTI

- K103N causes high-level resistance to NVP (~50-fold reduced susceptibility) and EFV (~20-fold reduced susceptibility). it has no effect on ETR or RPV susceptibility.
- V106M causes high-level resistance to NVP and EFV.

Other

- L210FS are rare mutations that are not associated with NRTI-resistance.

Annexure 2

PI resistance on failing 2nd line ART

Drug Resistance Interpretation: PR

PI Major Resistance Mutations:	**M46I, G48V, I54V, I84V, L90M**
PI Minor Resistance Mutations:	None
Other Mutations:	None

Protease Inhibitors

atazanavir/r (ATV/r)	High-level resistance
darunavir/r (DRV/r)	Potential low-level resistance
fosamprenavir/r (FPV/r)	High-level resistance
indinavir/r (IDV/r)	High-level resistance
lopinavir/r (LPV/r)	High-level resistance
nelfinavir (NFV)	High-level resistance
saquinavir/r (SQV/r)	High-level resistance
tipranavir/r (TPV/r)	Intermediate resistance

PR Comments

PIMajor

- M46I/L decreases susceptibility to IDV/r, NFV, FPV/r, LPV/r, and ATV/r when present with other mutations.
- G48V causes high-level SQV/r resistance, intermediate ATV/r and NFV resistance, and low-level IDV/r and LPV/r resistance.
- I54V contributes resistance to each of the PIs except DRV/r. It is synergistic with V82A/S/T in decreasing PI susceptibility.
- I84V causes intermediate/high-level resistance to ATV/r, FPV/r, IDV/r, NFV, and SQV/r; and low-level resistance to LPV/r, TPV/r, and DRV/r.
- L90M reduces susceptibility to NFV, SQV/r, ATV/r, and IDV/r. When present with other mutations it also reduces susceptibility to FPV/r and LPV/r.

Special

- This sequence has 1 major TPV/r-resistance mutations (I54V), 1 minor TPV/r-resistance mutations (I84V), and 0 mutations associated with increased TPV/r responsiveness. RESIST study (Baxter J et al J Virology 2006 and Scherer J et al EACS 2007).
- The following 1 of the 11 darunavir/r POWER/DUET study mutations were present: I84V (DeMeyer S et al, EHDRW 2008).