

SECTION 6

THERAPEUTIC DRUG MONITORING

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The objectives of this section are:

- To test your ability to monitor serum levels for drugs with a narrow therapeutic index
- To test your ability to interpret serum level results for drugs with a narrow therapeutic index
- To test your ability to adjust dosing regimens for drugs with a narrow therapeutic index in response to serum level results
- To test your ability to use the SUHT Department of Infection website to determine suitable dosing regimens for antibiotics that require therapeutic drug monitoring
- To test your ability to risk assess a patient with a possible penicillin allergy

INTRODUCTION

The first section of this workbook will test your ability to safely prescribe, monitor and adjust dosing of the following commonly prescribed drugs that require therapeutic drug monitoring (TDM):

- Phenytoin
- Carbamazepine
- Gentamicin
- Vancomycin
- Teicoplanin
- Lithium
- Digoxin
- Aminophylline / Theophylline

Work through the case studies and answer the questions using information resources available to you in your clinical practice environment.

The second section of the workbook will test your ability to evaluate a patient with a history of penicillin allergy and make a risk assessment for prescribing of penicillins and related antibiotics.

Question 1.1.3

Prescribe a suitable initial maintenance regimen for a 58kg patient on the regular section of the chart below.

DRUG (print approved name)	Dose		Additional info and/or dose/kg						
	mg	microgram		ml	units	09.00			
Signature	Date	Route	Pharmacy	13.00					
	Bleep			17.00					
Print name & designation				21.00					

Question 1.1.4

Describe your approach to monitoring serum phenytoin levels for your patient following loading and maintenance dosing. What time during the dose interval should blood samples be taken and how many days into therapy?

Question 1.1.5

Consult the BNF Section 4.8.1 and make a note below of the plasma concentration for optimum response for phenytoin.

Question 1.1.6

The patient's phenytoin serum level after 6 days of therapy at a maintenance dose of 300mg iv daily is reported as 25mg/L. List the possible reasons why this patient's phenytoin level appears high.

Question 1.1.7

The patient is suitable for oral maintenance therapy. Suggest an appropriate oral maintenance dose for this patient taking into consideration the recently reported high level.

Example 1.2

A 55-year-old male patient with a history of epilepsy is admitted with suspected pneumonia and started on co-amoxiclav and clarithromycin. His maintenance dose of phenytoin is 350mg orally once daily. Two days later, he complains of mouth discomfort and is prescribed fluconazole 50mg daily for oral thrush. Five days into the pneumonia treatment course, he develops nystagmus and slurred speech and your consultant suspects phenytoin toxicity.

Question 1.2.1

What action should be taken at this stage with regard to phenytoin therapy?

Question 1.2.2

The patient's serum phenytoin level is reported as 32mg/L. Consult the BNF Appendix 1 and identify any drug interactions that may account for the toxic phenytoin level.

Question 1.2.3

List the options for managing this patient's current problems (pneumonia, oral thrush and phenytoin toxicity).

2.0 CARBAMAZEPINE

Example 2.1

A 53-year-old lady under your care is diagnosed with trigeminal neuralgia and your consultant asks you to start her on carbamazepine.

Question 2.1.1

Prescribe an initial regimen of carbamazepine for trigeminal neuralgia for this patient on the chart below (BNF Section 4.8.1).

DRUG (print approved name)	Dose		Additional info and/or dose/kg						
	mg	microgram		ml	units	09.00			
Signature	Date		Route	Pharmacy	13.00				
	Bleep				17.00				
Print name & designation					21.00				

Question 2.1.2

Describe how dosing of carbamazepine should be titrated and why is titration required?

Question 2.1.3

Describe your approach to monitoring serum carbamazepine levels for your patient during titration and maintenance dosing. What time during the dose interval should blood samples be taken and how many days into therapy?

Question 2.1.4

Consult the BNF Section 4.8.1 and make a note below of the plasma concentration for optimum response for carbamazepine.

Example 2.2

A 21-year-old female medical student with a history of complex partial seizures due to temporal lobe epilepsy is referred to the hospital by her GP due to loss of seizure control. She has been maintained on Tegretol Retard tablets 600mg twice daily for over two years. A serum carbamazepine level is reported as 2.4mg/L.

Question 2.2.1

Consider the possible explanations for a low carbamazepine serum level in this patient and list the questions you would ask the patient or carer.

Question 2.2.2

Consult the BNF Appendix 1 and list the drugs that reduce carbamazepine serum levels.

Question 2.2.3

The patient reveals that she has been feeling low recently due to a family bereavement and failing several examinations and after consulting a community pharmacist, she was recommended St. John's Wort for depression. You note that St. John's Wort can reduce carbamazepine serum levels. What are the options for management of this patient's current problems (loss of seizure control and depression)?

Question 2.2.4

Treatment with St. John's Wort is stopped and the patient is started on fluoxetine. The patient is readmitted one week later with loss of seizure control and a carbamazepine serum level is reported at 8mg/L. What explanation can you offer for the loss of seizure control despite an apparently effective carbamazepine concentration and what are the options for management?

3.0 GENTAMICIN

Example 3.1

An adult inpatient under your care is diagnosed with pyelonephritis and a mid-stream urine specimen grows a Gram-negative organism sensitive to gentamicin. Your consultant instructs you to prescribe “once-daily” gentamicin for this patient.

Question 3.1.1

List the minimum information you require to prescribe a gentamicin regimen safely for your patient.

Question 3.1.2

Select an adult patient currently or previously under your care and record the information requested in Question 1 for this patient in the space below.

Question 3.1.3

Access the Department of Infection website from the SUHTranet homepage and select the link for gentamicin dosing. Using the information recorded above, select an initial dosing regimen for your patient and prescribe on the chart below.

DRUG (print approved name)	Dose		Additional info and/or dose/kg						
	mg	microgram		ml	units				
Signature	Date		Route	Pharmacy	09.00				
	Bleep				13.00				
Print name & designation					17.00				
					21.00				

Question 3.1.4

When is the first blood sample due to monitor the gentamicin level for this patient and what action will you take to ensure that the blood sample is taken at the correct time and the result interpretable?

Example 3.2

A 56-year-old male patient under your care is being treated with intravenous amoxicillin and gentamicin for an enterococcal infective endocarditis. On the fifth day of therapy, the patient is clinically stable but a pre-dose gentamicin serum level is reported as 3.2mg/L (target <1mg/L).

Question 3.2.1

List the possible reasons why this patient's gentamicin serum level appears high?

Question 3.2.2

If the level is confirmed as a true pre-dose level and the patient weighs 70kg and is currently prescribed 80mg 8-hourly, what action will you take to ensure continuing treatment is safe and effective?

Example 3.3

An adult patient under your care is on day 8 of gentamicin therapy for a Gram-negative hospital-acquired pneumonia. The patient was prescribed 5mg/kg once daily and a gentamicin serum level is reported as 10mg/L.

Question 3.3.1

Access the Department of Infection website from the SUHTranet homepage and select the link for gentamicin dosing. What information is required in order to interpret the gentamicin serum level for this patient?

Question 3.3.2

If the required information is not available to you, what options are available to you to guide clinical management of the patient?

Example 3.4

A 79-year-old female patient under your care develops Gram negative bacteraemia from a suspected urinary source. The organism is only sensitive to gentamicin but your patient has poor renal function. She weighs 52kg and her recent serum creatinine is 191micromol/L.

Question 3.4.1

Access the Department of Infection website from the SUHTranet homepage and select the link for gentamicin dosing. Use the link to the on-line creatinine clearance calculator to estimate creatinine clearance for this patient and record below.

Question 3.4.2

Select an appropriate dosing regimen for this patient and prescribe below.

DRUG (print approved name)	Dose		Additional info and/or dose/kg						
	mg	microgram		ml	units	09.00			
Signature	Date	Route	Pharmacy	13.00					
	Bleep			17.00					
Print name & designation				21.00					

Question 3.4.3

Suggest an appropriate serum level monitoring strategy for this patient and provide the target range(s) below.

4.0 VANCOMYCIN

Example 4.1

An adult patient under your care following cardiac surgery develops a sternal wound infection and a deep specimen grows MRSA. The consultant microbiologist recommends a course of vancomycin.

Question 4.1.1

List the minimum information you require to prescribe a vancomycin regimen safely for your patient.

Question 4.1.2

Select an adult patient currently or previously under your care and record the information requested in Question 1 for this patient in the space below.

Question 4.1.3

Access the Department of Infection website from the SUHTranet homepage and select the link for vancomycin dosing. Using the information recorded above, select an initial dosing regimen for your patient and prescribe on the chart below.

DRUG (print approved name)	Dose		Additional info and/or dose/kg					
	mg	microgram						
Signature				09.00				
				13.00				
Print name & designation	Date	Route	Pharmacy	17.00				
	Bleep			21.00				

Question 4.1.4

When is the first blood sample due to monitor the vancomycin level for this patient and what action will you take to ensure that the blood sample is taken at the correct time and the result interpretable?

Example 4.2

A 34-year-old male patient under your care is on day 6 of a course of iv vancomycin and gentamicin therapy for right-sided infective endocarditis due to viridans streptococci. The patient is penicillin-allergic and an illicit intravenous drug user. He was prescribed 1gram twice daily but a pre-dose serum level is reported as 7.4mg/L.

Question 4.2.1

List the possible reasons why this patient's vancomycin serum level appears low?

Question 4.2.2

Access the Department of Infection website from the SUHTranet homepage and select the link for vancomycin dosing. What is the target pre-dose level for this patient?

Question 4.2.3

If the level is confirmed as a true pre-dose level, what action will you take to ensure continuing treatment is safe and effective?

5.0 TEICOPLANIN

Example 5.1

A 67-year-old female patient with a history of diabetes and chronic renal failure is admitted with severe sepsis from an infected foot ulcer and a deep wound specimen grows MRSA. The microbiologist recommends teicoplanin in view of the patient's poor renal function.

Question 5.1.1

Access the Department of Infection website from the SUHTranet homepage and select the link for renal dosing. This patient is 5'1" tall and weighs 92kg. Her serum creatinine is 266micromol/L. Calculate her ideal body weight and creatinine clearance and record below.

Question 5.1.2

Access the UK electronic medicines compendium (EMC) at www.medicines.org.uk and view the monograph for teicoplanin injection (Targocid). Consult section 4.2 "Posology and method of administration" and prescribe a safe and effective teicoplanin regimen for this patient on the chart below, indicating on the administration section when doses are to be given.

DRUG (print approved name)	Dose		Additional info and/or dose/kg					
	mg	microgram		ml	units			
Signature				09.00				
				13.00				
Print name & designation	Date	Route	Pharmacy	17.00				
	Bleep			21.00				

Question 5.1.3

How will the dosing regimen be adjusted to account for this patient's renal impairment?

Question 5.1.4

When should a blood sample be taken for teicoplanin serum levels (EMC monograph Section 5.2) and what is the BNF recommended target serum level?

6.0 LITHIUM

Example 6.1

A 36-year-old male patient with a history of bipolar disorder controlled with lithium is admitted with coarse tremor and loss of co-ordination. The patient is maintained on lithium slow release tablets (Priadel) 400mg twice daily. A serum lithium level is reported as 1.4mmol/L.

Question 6.1.1

What is the recommended serum concentration range for lithium in the BNF?

Question 6.1.2

Consult BNF Section 4.2.3 and record the advice recommended for management of mild cases of lithium toxicity.

Question 6.1.3

List the possible explanations for this patient's high lithium level and what questions you will ask the patient.

Question 6.1.4

The patient admits to borrowing some of his mother's arthritis tablets for a migraine that had been bothering him for several days. Check the BNF Appendix 1 and list the possible drugs that interact with lithium that are also used for symptomatic relief of arthritis.

Question 6.1.5

How should this patient be managed once the lithium toxicity has resolved.

7.0 DIGOXIN

Example 7.1

A 74-year-old woman is admitted with shortness of breath in atrial fibrillation. The consultant on the post-take ward round asks you to prescribe a digoxin oral loading dose and maintenance regimen.

Question 7.1.1

What information should be taken into consideration when prescribing a loading and maintenance dose for digoxin?

Question 7.1.2

Suggest an appropriate loading regimen and maintenance regimen for this patient depending on the information listed in the previous question.

Question 7.1.2

How does the BNF suggest that the maintenance dose of digoxin be determined in practice (Section 2.1.1) and what is the recommended target serum concentration?

Question 7.1.3

Ten days after starting digoxin therapy at a maintenance dose of 125micrograms daily, the patient's resting ventricular rate is stable at around 80bpm and her shortness of breath has resolved. However, she suffers a stroke and is having difficulty swallowing and a naso-gastric tube is inserted. Prescribe the digoxin in liquid form on the chart below.

DRUG (print approved name)	Dose		Additional info and/or dose/kg					
	mg	microgram		ml	units			
Signature				09.00				
				13.00				
Print name & designation	Date	Route	Pharmacy	17.00				
	Bleep			21.00				

Question 7.1.4

A serum digoxin concentration after 14 days of therapy is reported as 3microgram/L but the patient appears to be clinically stable with no apparent signs of toxicity. Suggest some explanations for the reported serum concentration.

Question 8.1.3

When should a blood sample be taken to measure serum theophylline levels and what is the desired therapeutic range?

Question 8.1.4

The patient develops severe nausea and vomiting along with tachycardia and a serum theophylline level is reported as 32mg/L. List the possible explanations for the high theophylline level.

Question 8.1.5

A family member confirms that the patient regularly takes Slo-Phyllin and the aminophylline infusion is stopped. What is the typical half-life of theophylline and how long would you expect to wait before restarting the infusion?

Question 8.1.6

The patient's condition stabilizes and the consultant asks you to stop the aminophylline infusion and convert the patient to oral theophylline. Suggest an approach to managing the crossover from intravenous to oral agents and prescribe an appropriate oral regimen on the chart below.

DRUG (print approved name)	Dose		Additional info and/or dose/kg						
	mg microgram ml units			09.00					
Signature	Date	Route	Pharmacy	13.00					
					17.00				
Print name & designation	Bleep			21.00					

Question 8.1.7

The patient develops a catheter-associated urinary tract infection and microbiology recommends ciprofloxacin. Evaluate the potential for interaction between ciprofloxacin and theophylline in this patient and suggest an approach to future management of drug therapy.

SECTION B – PENICILLIN ALLERGY

Example B1

A 14-year-old boy is admitted with rapidly-spreading cellulitis after sustaining a bruise playing rugby. The surgical registrar is called and agrees to attend urgently and asks you to start intravenous benzylpenicillin and flucloxacillin. The boy's mother reports a history of penicillin allergy.

Question B1.1

What questions should you ask to fully elucidate the nature of the reported allergy.

Question B1.2

The patient's mother recalls a rash developing on the boy's trunk several days after starting a course of amoxicillin for an ear infection when the patient was 5 years old but she is reasonably certain that he has since received penicillin V for a throat infection with no ill effects. How will you proceed and why?

Example B2

A 40-year-old woman is admitted with moderately severe community-acquired pneumonia. She reports a history of an urticarial rash and shortness of breath shortly after starting a course of penicillin for a sore throat several years ago, after which her GP advised her to avoid penicillin antibiotics.

Question B2.1

Suggest an antibiotic regimen for this patient and explain your rationale.

Question B2.3

A blood culture for this patient is positive for *Streptococcus pneumoniae*, sensitive to the following drugs: Penicillin, amoxicillin, cefotaxime, cefuroxime, co-amoxiclav, Tazocin, doxycycline and vancomycin

Which of these antibiotics is safe to use in this patient?

End of Section 6.

F1Doctor
Signature.....GMC.....

F2Doctor
Signature.....GMC.....