Exercises in CLINICAL ACCURACY CHECKING

By ALISON EGGLETON, MSc, MRPHARMS, *and* BRIT CADMAN, BPHARM, MRPHARMS

These checking exercises attempt to address the pharmaceutical and medical issues that arise in different specialties. The prescriptions in this issue have been selected to illustrate common antibiotic-related questions that may be identified when prescriptions arrive in the dispensary. Readers are invited to identify the problems and determine solutions for them.

Mrs Eggleton is principal pharmacist, education and training, and Ms Cadman is principal clinical pharmacist, at Addenbrooke's Hospital, Cambridge

The prescriptions are followed by a discussion of the significant issues.

It must be emphasised that these tests were introduced to assess the performance of checkers in a dispensary situation where time is at a premium. It should also be noted that these prescriptions have passed through the dispensary at Addenbrooke's NHS Trust, although the patients' names have been removed to maintain confidentiality. The check list used by candidates is shown in Figure 1. Figure 2 (p300) relates to prescription 1, Figure 3 (p300) relates to prescription 2 and Figure 4 (p302) relates to prescription 3.

CLINICAL ACCURACY CHECKING TEST

Task

1. You have **– minutes** to review the following prescription charts and identify the problems. You have **– minutes** to document your answers

Total time allowed: – minutes

2. You are only able to make ONE intervention per prescription

For each of the prescriptions, using the answer sheets provided:

3. Document the ward and clinical specialty
4. List briefly the endorsements you would make to the chart
5. List briefly the patient's major medical problem(s) suggested by the drug therapy
6. List briefly the most important pharmaceutical problems you would try to resolve **if you were checking the chart on a ward** (maximum of **SIX** problems)
7. State the **ONE priority intervention** you would make for **EACH of the charts** given that you are **checking the chart in the dispensary** (NB: Occasionally, more than one intervention may be needed)
8. Briefly state the **action** you would take to resolve the priority intervention
9. State the urgency of the **priority** intervention from one of the following:

Urgent = chart must be amended by a doctor or pharmacist before being dispensed

Less urgent = any other action, such as sending an intervention note to the doctor, highlighting the problem to the ward pharmacist, telephoning a nurse or doctor for further information

10. Materials allowed:

Martindale's Extra Pharmacopoeia	BNF
Paediatric formulary	Hospital formulary
Compendium of data sheets and SPCs	Calculator
Trissel's handbook of injectable drugs	Hospital IV monographs
Renal drug handbook	

List of wards — specialty and current ward pharmacist

Answer sheet (Candidate name:.....)

Prescription number 1

Review panel:

Ward Clinical specialty

Chart endorsements:

Medical problems:

1.	5.
2.	6.
3.	7.
4.	8.

Pharmaceutical problems:

1.	4.
2.	5.
3.	6.

Priority intervention number 1 2 3 4 5 6
(circle the appropriate number)

Suggested action to resolve the priority intervention:

Urgency: Urgent Less urgent
(circle as appropriate)

Figure 1: Instructions for candidates: state the ward and clinical specialty in order to focus attention on likely problems. For example, if the patient was on a medical ward specialising in renal disease, the pharmacist must be particularly vigilant about renally excreted drugs. The chart endorsements refer to the discharge or to take out (TTO) prescription where one exists or otherwise to the inpatient chart. Please note: candidates are given six minutes to review each prescription, and three minutes to document their answers for each prescription

Prescription Chart

Surname	Hospital No	Weight	DRUG SENSITIVITIES
P	334455		Doctor must also enter this information on FRONT of case folder must not be administered unless this box has been completed — Drugs must not be administered unless this box has been completed
First Names	Date of Birth / Sex		Date / Drug/Substance / Signature
T	14.03.53 / F		14.09.02 / NKDA / A DOCTOR
Consultant	Ward	Height	
	Medical		

Regular Prescriptions

Month and date → 14 | 15 | 16 | 17 | 18

Tick times or enter other times →

DRUG (APPROVED NAME)	Dose	Route	Start Date	Stop Date	Signature	Pharm	Additional Instructions	Time	*	14	15	16	17	18
Cefotaxime	1g	IV	14.09.02		A Doctor			6						
								8	*		AN	AN		
								12						
								14	*	AN	AN			
								18						
								22	*	AN	AN			
Metronidazole	500mg	IV	14.09.02		A Doctor			6						
								8	*		AN	AN		
								12						
								14	*		AN	AN		
								18						
								22	*	AN	AN			
Cephalexin	250mg	PO	16.09.02		A Doctor			6	*					
								8						
								12	*					
								14						
								18	*					
								22	*					
Metronidazole	400mg	PO	16.09.02		A Doctor			6						
								8	*					
								12						
								14	*					
								18						
								22	*					

Figure 2: Patient's details and regular drugs (prescription 1). Double-headed arrow indicates discontinuation

Prescription Chart

Surname	Hospital No	Weight	DRUG SENSITIVITIES
L	445566		Drugs
First Names	Date of Birth / Sex		Date / Drug/Substance / Signature
C	27.05.25 / M		09.09.02 / NKDA / A DOCTOR
Consultant	Ward	Height	
	Surgical		

Regular Prescriptions

Month and date → 09 | 10 | 11 | 12 | 13

Tick times or enter other times →

DRUG (APPROVED NAME)	Dose	Route	Start Date	Stop Date	Signature	Pharm	Additional Instructions	Time	*	09	10	11	12	13
Flucloxacillin	1g	IV	09.09.02		A Doctor			6	*		AN	AN	AN	
								8						
								12	*	AN	AN	AN		
								14						
								18	*	AN	AN	AN		
								22	*	AN	AN	AN		
Benzylpenicillin	1.2g	IV	09.09.02		A Doctor			6	*		AN	AN	AN	
								8						
								12	*	AN	AN	AN		
								14						
								18	*	AN	AN	AN		
								22	*	AN	AN	AN		
Clindamycin	600mg	IV	12.09.02		A Doctor			6						
								8	*					
								12						
								14						
								18	*					
								22						
Erythromycin	500mg	IV	12.09.02		A Doctor			6						
								8	*					
								12	*					
								14						
								18	*					
								22	*					

Figure 3: Patient's details and regular drugs (prescription 2). Double-headed arrow indicates discontinuation

Prescription 1

Figure 5 (p303) shows the solution to prescription 1. This prescription for Mrs PT highlights the problem of the appropriate conversion between oral and intravenous routes of administration for antibiotics. This type of prescription is commonly seen in hospitals, although here it has been simplified in order to illustrate the antibiotic-related problem.

The type of infection suffered by a patient can often be predicted by the pharmacist from the antibiotic regimen prescribed. There are published data on the types of organism most likely to cause particular infections. For example, if this patient had hospital-acquired pneumonia, we would know that the infection results from microaspiration of oropharyngeal secretions, and the most likely causative organisms are pathogens found in these secretions, such as *Staphylococcus aureus* and Gram-negative bacilli.[1] If the patient is at risk of gross aspiration, for example, due to impaired consciousness or impaired gag reflex, there is an increased risk of infection with anaerobic organisms. A "best guess" antibiotic regimen, therefore, should include antibiotics likely to cover this range of pathogens. The hospital microbiology department should keep data on local infection patterns, with associated local bacterial resistance, and should produce antibiotic treatment guidelines. Third generation cephalosporins have the advantage over first- and second-generation drugs in having better *in vitro* activity against Gram-negative aerobic organisms.[2] They have some activity against *S aureus* (though less than second-generation drugs[3]) and streptococci, and may have some activity against anaerobic respiratory pathogens,[2] although metronidazole is commonly added to regimens for this purpose. Addenbrooke's Hospital is perhaps slightly unusual in its use of cefotaxime as a first-line intravenous antibiotic.

Without being able to check the patient's admission notes or speak to the doctor, the dispensary pharmacist cannot be certain of the infection being treated. Prophylaxis against aspiration pneumonia is one possibility, but there are others, such as intra-abdominal infections like cholecystitis (acute inflammation of the gall bladder).[4] In converting to oral medication, however, knowledge of the type of infection being treated and the site of infection are important. The oral antibiotic should cover a similar range of likely causative organisms and should also penetrate to the infection site in an effective concentration. Here there is a problem because cefotaxime is not available in an oral formulation. In fact, no third generation oral cephalosporin is on the formulary at Addenbrooke's. This may be because of limited antibacterial action. Cefixime, for example, has no activity against *S aureus* or anaerobes, and has decreased activity against *S pneumoniae*[2] and other streptococcal species.[5] First and second generation cephalosporins also lack the same range of antibacterial activity. Cefalexin (first-generation) is excreted in high concentration in the urine[6] and is considered by the microbiologists at Addenbrooke's to be effective principally in urinary tract infections. [Readers who are linked to NHSnet can visit **nww.addenbrookes-pharmacy.nhs.uk** to view the Addenbrooke's Hospital antibiotic guide.] In a dose of 250mg four times a day, cefalexin would not be effective against soft-tissue infections despite its good oral absorption.[2] In changing from the intravenous to the oral route, therefore, it may be necessary to change to a different class of antibiotics, rather than converting to an oral cephalosporin. One option frequently used at Addenbrooke's is to convert to oral ciprofloxacin, remembering that ciprofloxacin, although broad spectrum and with good tissue penetration characteristics, also has reduced activity against some bacterial species, such as some species of streptococci and staphylococci.[7] The conversion from intravenous to oral metronidazole poses little problem because oral absorption is good and serum levels following equivalent oral and intravenous doses are similar.[8,9] However, another option might be to convert to oral co-amoxiclav alone. Co-amoxiclav has activity against a wide range of Gram-positive and Gram-negative aerobic and anaerobic bacterial species.[10]

A competent pharmacist should be expected to recognise that conversion from a third generation to a first generation cephalosporin might not produce the same spectrum of antimicrobial activity or tissue penetration. More experienced pharmacists might be able to discuss the likely causative organisms of common infections, predict the type of infection from the antibiotic regimen prescribed and be aware of limitations in the spectrum of activity of common antibiotics.

Prescription 2

Prescription 2 illustrates the problem of the appropriate use of a potentially toxic antibiotic and the appropriate combination of antibiotics. The solution to this problem can be found in Figure 6 (p304).

In the prescription, the likely infection being treated is, perhaps, more obvious. Community-acquired cellulitis, an acute infection of the skin involving subcutaneous tissues, is most likely to be caused by *S aureus* or group A betahaemolytic streptococci in adults.[11] It is commonly treated with benzylpenicillin, effective against many streptococci, and flucloxacillin, effective against penicillin-resistant staphylococci.[3] If the patient has been admitted to hospital with cellulitis, it is usually indicative of a severe infection. The intravenous route is often used initially to ensure penetration of the drug to the affected site in an effective concentration. Conversion to the oral route usually occurs once there are clinical signs of improvement, such as regression of the area of inflammation.

After three days of intravenous antibiotic therapy, rather than conversion to the oral route of administration, Mr CL has been changed to a different intravenous drug regimen. Cellulitis can be found in more severe forms, such as deeper, necrotising infections that involve rapidly progressive inflammation and necrosis of the skin, subcutaneous fat and fascia, and possibly muscle,[11] often accompanied by systemic symptoms. In this type of infection, the range of likely causative organisms is different, and includes streptococci (groups A and B particularly), *S aureus*, Gram-negative organisms and anaerobes.

The main problem in this patient is that antagonism has been demonstrated *in vitro* between clindamycin and erythromycin.[12] Both antibiotics bind to the 50S subunit of bacterial ribosomes and suppress protein synthesis. Because they act at sites within close proximity, binding by one antibiotic can inhibit the interaction of the other antibiotic with its receptor site. Co-administration is not recommended because of the possible clinical significance of this interaction.[13]

Clindamycin is the most effective antibiotic with activity against group A streptococci[11] but it is also effective against other streptococcal species, methicillin-sensitive strains of *S aureus*, and some anaerobic bacteria such as *Bacteroides fragilis*.[11] It is generally reserved for severe infections because of its side effects. In Mr CL's prescription the dose is quite low. In necrotising fasciitis, for example, a dose of 600mg four times a day would be more usual. The incidence of antibiotic-induced colitis limits the use of clindamycin to infections where it is clearly superior to other antibiotic agents. Erythromycin is also effective against group A streptococci[14] but significant resistance has been reported in some areas.[13] Methicillin-sensitive strains of *S aureus* are generally sensitive, although resistance may emerge during therapy and *B fragilis* is usually resistant, although erythromycin has some activity against other Gram-negative anaerobes. Therefore, in severe infection, clindamycin would appear to be the drug of choice.

Where a drug such as clindamycin has been prescribed, it is reasonable to expect that a competent dispensary pharmacist should check with the prescribing doctor whether or not microbiological culture and sensitivity data are available to support the drug regimen selected, and whether or not advice has been sought from a microbiologist. A more experienced pharmacist might have known about the *in vitro* drug interaction between erythromycin and clindamycin and questioned their concurrent administration. The

Prescription Chart

Surname	Hospital No	Weight	DRUG SENSITIVITIES
S	556677		Doctor must also enter this information on FRONT of case folder must not be administered unless this box has been completed. Drugs
First Names	Date of Birth / Sex		Date / Drug/Substance / Signature
K	21.06.76 / M	Height	04.08.02 / NKDA / A DOCTOR
Consultant	Ward		
	Medical		

Regular Prescriptions

Month and date / Tick times or enter other times

DRUG (APPROVED NAME)	Dose	Route	Start Date	Stop Date	Signature	Pharm	Additional Instructions			4	5	6	7	8
Phenytoin	300mg	PO	04.08.02		A Doctor			6						
								8						
								12						
								14						
								18						
								22	*	AN	AN	AN	AN	
Baclofen	20mg	PO	04.08.02		A Doctor			6						
								8	*		AN	AN	AN	AN
								12						
								14	*	AN	AN	AN	AN	
								18						
								22	*	AN	AN	AN	AN	
Paracetamol	1g	PO	04.08.02		A Doctor			6	*		AN	AN	AN	AN
								8						
								12	*	AN	AN	AN	AN	
								14						
								18	*	AN	AN	AN	AN	
								22	*	AN	AN	AN	AN	
Ciprofloxacin	200mg	IV	08.08.02		A Doctor			6						
								8	*					AN
								12						
								14						
								18	*					
								22						

Figure 4: Patient's details and regular drugs (prescription 3)

dispensary pharmacist should also ensure that the appropriate intravenous drug monographs are available on the ward for the antibiotic regimen eventually selected.

Prescription 3

The question raised in prescription 3 is whether or not the intravenous route is the appropriate one for the antibiotic prescribed. Figure 7 (p304) shows the solution to this problem posed in prescription 3.

In this patient, we are again unaware of the exact type of infection. Ciprofloxacin has good activity against Gram-negative bacteria, including *Pseudomonas aeruginosa*, and Gram-positive organisms although it is known to be less active against some streptococci (*Enterococcus faecalis, Streptococcus pneumoniae, S pyogenes, S viridans*), and other organisms including *Mycoplasma* species and *Chlamydia* species.[7] It is often prescribed alone in complicated urinary tract infections, although in respiratory tract infections it is usually used in combination with benzylpenicillin to try to improve streptococcal cover. However, it has a wide range of other licensed indications.[7] The two concerns for the patient are the appropriateness of using the intravenous route of administration and caution in the use of quinolone antibiotics in patients with epilepsy.

The oral bioavailability of ciprofloxacin is reported variously in the literature as 60 ± 12 per cent,[15] 60–80 per cent[16] and 52–83 per cent.[7] Peak plasma concentrations are reported to occur at 30 to 90 minutes after oral dosing and at the end of the infusion period (30 minutes for a 100mg or 200mg dose, 60 minutes for a 400mg dose) for intravenous dosing.[7] Plasma concentrations are reported as 3 ± 0.6mg/l from an oral dose of 750mg, and 3.2 ± 0.6mg/l from an intravenous dose of 200mg.[16] It would therefore appear that an equivalent effect may be achieved using the oral route as long as a higher dose is used. At Addenbrooke's, it is taken that a 200mg intravenous dose is approximately equivalent to a 250 to 500mg oral dose. There is a significant cost difference between the intravenous and oral preparations.[3] In addition, the intravenous route carries a much greater risk for the patient, because of for example, risk of infection through the IV line, miscalculation of dose and wrong speed of administration. The intravenous route is, however, recommended for serious or life-threatening infections such as sepsis or infection in a neutropenic patient. Therefore the dispensary pharmacist might contact the prescriber to check on the nature of the infection in this patient and question whether ciprofloxacin might be administered orally, say in a dose of 500mg twice daily, since the patient is taking all other medications orally.

Ciprofloxacin has been known to cause fitting in a small number of patients with or without epilepsy.[3,17] The British National Formulary mentions a Committee of Safety of Medicines warning of the risk of ciprofloxacin-induced convulsions, particulary if non-steroidal anti-inflammatory drugs (NSAIDs) are taken at the same time.[3] The manufacturer lists central nervous system adverse effects, including convulsions, and states that ciprofloxacin may alter serum phenytoin concentrations.[7] Stockley mentions isolated case reports where phenytoin concentrations have fallen in patients started on ciprofloxacin but states that blood levels are usually unaffected.[17] Therefore, there is the possibility of either a drug-drug or drug-disease interaction.[7,17] In planning pharmaceutical care, the pharmacist must always act in the interest of the patient, considering factors such as cure of the disease but also quality of life. In advising about the use of ciprofloxacin in a patient with epilepsy, the pharmacist should be able to advise doctor and patient on risk versus benefit. The incidence of seizures has been reported to be less than 1 per cent.[16] Therefore, in a serious infection where a quinolone is drug of choice, the doctor and patient may jointly decide to proceed with therapy. There should be informed consent of the patient, however, since the consequences of an epileptic fit to the patient's quality of life may be serious. It could lead, for example, to the withdrawal of a driver's licence.

A competent pharmacist should be aware of the possibility of suggesting the oral route of administration of ciprofloxacin to the doctor. Pharmacists must also be aware of including both doctor and patient in decisions about drug therapy.

References

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Exercises in clinical accuracy checking

Exercises in clinical accuracy checking have been appearing in *Hospital Pharmacist* since June 2000. The idea for the series came from Alison Eggleton, principal pharmacist, education and training at Addenbrooke's Hospital, Cambridge. Since then, all the exercises have been taken from actual prescriptions presented to the dispensary at Addenbrooke's Hospital.

Starting in 2003, *Hospital Pharmacist* would like to extend the series by asking pharmacists at other hospitals to submit pharmaceutical problems seen in their hospitals.

General advice for contributors can be found at **www.pjonline.com** but it has to be stressed that authors must also be aware that the problems are to assess the performance of checkers in a dispensary situation where time is at a premium. It should not take candidates more than six minutes to review each prescription, and three minutes to document their answers for each prescription.

Answer sheet (answers are shown in magenta) Candidate name:.....

Prescription number 1

Ward: Medical Clinical specialty: Medical

Chart endorsements:
Metronidazole — after food, swallow with plenty of water

Medical problems:
Infection; broad spectrum cover required

Pharmaceutical problems:
1. Change from IV antibiotics to oral; maintenance of spectrum of cover against different bacterial species

Priority intervention Number 1

Suggested action to resolve the priority intervention:
Check the type of infection being treated with IV antibiotics. Ensure that the oral antibiotics are likely to cover a similar range of likely causative organisms and are likely to penetrate to the affected site in adequate concentrations

Urgency: Less urgent

Figure 5: Solution to prescription 1

Answer sheet (answers are shown in magenta) Candidate name:.....

Prescription number 2

Ward: Surgical Clinical specialty: Surgical

Chart endorsements:
1. Clindamycin — give over at least 10–60 minutes
2. Erythromycin — give over 20–60 minutes
3. Flucloxacillin — give over 30–60 minutes
4. Benzylpenicillin — give over 30–60 minutes

Medical problems:
Infection — possibly cellulitis

Pharmaceutical problems:
1. Concurrent use of erythromycin and clindamycin is not recommended
2. Appropriate prescribing of clindamycin
3. Risk of pseudomembranous colitis, particularly using clindamycin

Priority intervention Number 1

Suggested action to resolve the priority intervention:
Check that a microbiologist recommended the use of clindamycin following appropriate microbiological culture and sensitivity tests. Seek microbiologist's advice on an appropriate antibiotic regimen.

Urgency: Urgent

Figure 6: Solution to prescription 2

Answer sheet (answers are shown in magenta) Candidate name:.....

Prescription number 3

Ward: Medical Clinical specialty: Medical

Chart endorsements:
Phenytoin — with plenty of water

Medical problems:
1. Infection
2. Epilepsy
3. Muscle spasms
4. Pain or fever

Pharmaceutical problems:
1. Ciprofloxacin — caution in patients with epilepsy
2. Intravenous administration in a patient able to take oral medication

Priority intervention Number 2

Suggested action to resolve the priority intervention:
Contact the doctor to discuss the appropriateness of the intravenous route of administration
Be prepared with data on comparative oral and IV bioavailability for ciprofloxacin

Urgency: Less urgent

Figure 7: Solution to prescription 3