

# Exercises in CLINICAL ACCURACY CHECKING

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**T**hese clinical accuracy checking exercises attempt to address the pharmaceutical and medical problems that arise in different specialties. The prescriptions in this issue deal with the use of drugs on the neurosurgery and neurology wards. Readers are invited to identify the problems and

determine solutions for them. The prescriptions are followed by a discussion of the significant issues raised.

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 (p244) relates to prescription 1, and Figure 3 (p244) relates to prescription 2.

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## 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:

- Document the ward and clinical specialty
- List briefly the endorsements you would make to the chart
- List briefly the patient's major medical problem(s) suggested by the drug therapy
- List briefly the most important pharmaceutical problems you would try to resolve **if you were checking the chart at ward level** (maximum of **SIX** problems)
- 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)
- Briefly state the **action** you would take to resolve the priority intervention
- 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's 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		
E			918273						Doctor must also enter this information on FRONT of case folder must not be administered unless this box has been completed		
First Names			Date of Birth			Sex			Date		
F			15.6.44			M			28.1.02		
Consultant			Ward			Height			Drug/Substance		
*****			Neurosurgery						CYCLIZINE (palpitation and vomiting)		
									Signature		
									A DOCTOR		
Regular Prescriptions						Regular Prescriptions					
Month and date						Month and date					
Tick times or enter other times						Tick times or enter other times					
DRUG (APPROVED NAME)						DRUG (APPROVED NAME)					
Enalapril						Dispersible aspirin					
Dose						Dose					
Route						Route					
Start Date						Start Date					
Stop Date						Stop Date					
Signature						Signature					
Pharm						Pharm					
Additional Instructions						Additional Instructions					
6						6					
8 *						8 *					
12						12					
14						14					
18						18					
22						22					
DRUG (APPROVED NAME)						DRUG (APPROVED NAME)					
Atenolol						Simvastatin					
Dose						Dose					
Route						Route					
Start Date						Start Date					
Stop Date						Stop Date					
Signature						Signature					
Pharm						Pharm					
Additional Instructions						Additional Instructions					
6						6					
8 *						8					
12						12					
14						14					
18						18					
22						22 *					
DRUG (APPROVED NAME)						DRUG (APPROVED NAME)					
Gliclazide						Atenolol					
Dose						Dose					
Route						Route					
Start Date						Start Date					
Stop Date						Stop Date					
Signature						Signature					
Pharm						Pharm					
Additional Instructions						Additional Instructions					
6						6					
8 *						8 *					
12						12					
14						14					
18						18					
22						22					

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

Prescription Chart											
Surname			Hospital No			Weight			DRUG SENSITIVITIES		
S			192837						Doctor must also enter this information on FRONT of case folder must not be administered unless this box has been completed		
First Names			Date of Birth			Sex			Date		
J			2.7.40			M			9.1.02		
Consultant			Ward			Height			Drug/Substance		
*****			Neurology						NKDA		
									Signature		
									A DOCTOR		
Regular Prescriptions						Regular Prescriptions					
Month and date						Month and date					
Tick times or enter other times						Tick times or enter other times					
DRUG (APPROVED NAME)						DRUG (APPROVED NAME)					
Carbamazepine						Carbamazepine					
Dose						Dose					
Route						Route					
Start Date						Start Date					
Stop Date						Stop Date					
Signature						Signature					
Pharm						Pharm					
Additional Instructions						Additional Instructions					
6						6					
8 *						8 *					
12						12					
14						14					
18						18 *					
22						22					
DRUG (APPROVED NAME)						DRUG (APPROVED NAME)					
Sodium valproate						Sodium valproate					
Dose						Dose					
Route						Route					
Start Date						Start Date					
Stop Date						Stop Date					
Signature						Signature					
Pharm						Pharm					
Additional Instructions						Additional Instructions					
6						6					
8 *						8 *					
12						12					
14						14 *					
18						18					
22						22 *					
DRUG (APPROVED NAME)						DRUG (APPROVED NAME)					
Domperidone											
Dose						Dose					
Route						Route					
Start Date						Start Date					
Stop Date						Stop Date					
Signature						Signature					
Pharm						Pharm					
Additional Instructions						Additional Instructions					
6						6					
8 *						8					
12						12					
14						14 *					
18						18					
22						22 *					

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

## PRESCRIPTION 1

Figure 4 (p247) shows the solution to prescription 1. This prescription from a neurosurgery ward is likely to be for a patient about to undergo carotid endarterectomy. Carotid endarterectomy is a surgical treatment in which atheromatous plaque is stripped from carotid vessels. It is recommended for patients suffering transient ischaemic attacks (TIAs)<sup>1</sup> where carotid stenosis is measured at greater than 70 per cent and for patients suffering a carotid area stroke with minor or absent residual disability.<sup>2</sup> TIAs, which are often due to atherothromboembolism of the internal carotid artery, are episodes of transient ischaemia of some part of the cerebral hemispheres or the brain stem lasting between minutes and hours. However, they are usually followed by complete recovery.<sup>3</sup> Symptoms include disturbed balance, temporary blindness, language disturbance, dysarthria, unsteadiness, confusion and a range of other signs depending on the site affected by the ischaemia.<sup>4</sup> The rate of onset of symptoms is usually more rapid than the rate of recovery. The disease may progress in some patients, with the combined risk of stroke, myocardial infarction or vascular death being about 10 per cent per annum.<sup>4</sup> In 50 per cent of patients who develop a stroke, progression will occur within a month of the TIA.

Carotid endarterectomy combined with appropriate medical treatment has been shown in clinical trials in the United States and Canada (NASCET<sup>5</sup>) and in Europe (ECST<sup>6</sup>) to reduce the risk of ipsilateral stroke in patients with symptomatic severe carotid artery stenosis. Surgery should be performed by experienced surgeons who have documented perioperative morbidity and mortality rates similar to those noted in the two studies. This procedure is usually only performed in specialist neurology centres. However, the principles applying to the changes in drug therapy equally apply to a patient being treated medically for TIAs.

The immediate goal of therapy in TIAs is to re-establish adequate blood flow in diseased cerebral vessels.<sup>7</sup> Long-term medical management involves reducing the risk of stroke, myocardial infarction and cardiac death (which can occur within hours, weeks or years of a TIA<sup>4</sup>) by controlling treatable risk factors. Abnormal blood glucose levels should be controlled even in the absence of symptomatic diabetes mellitus. The patient should be encouraged to stop smoking, lose any excess weight, if possible, and undertake exercise. Blood cholesterol requires control either by diet<sup>4</sup> or the use of cholesterol-lowering drugs in patients with a history of both ischaemic heart disease and a serum cholesterol greater than 5mmol/L following a stroke.<sup>2</sup> The ward pharmacist may be involved in patient counselling on lifestyle factors on admission and before discharge.

Approximately 90 per cent of strokes are due to uncontrolled hypertension, and stroke prevention involves the management of both systolic and diastolic blood pressure.<sup>7</sup> Diastolic blood pressure should be lowered gradually, initially to about 100mmHg<sup>4</sup> using non-drug measures or using drugs with caution, particularly in the elderly or those with severe arterial stenosis, because of the risk of cerebral hypoperfusion and postural hypotension<sup>4</sup> which could lead to a decreased level of consciousness or infarction.<sup>7</sup>

The eventual aim of blood pressure management in secondary stroke prevention in a diabetic patient is to reduce blood pressure to the target of systolic blood pressure under 140mmHg and diastolic blood pressure under 85mmHg.<sup>2</sup> A mild degree of hypertension may be acceptable in the short-term to overcome severe stenosis and maintain cerebral perfusion.<sup>7</sup>

Although the guidelines from the Royal College of Physicians (RCP) support the management of hypertension,<sup>2</sup> there is a problem with drug selection in this patient. The guidelines state that hypertension persisting for more than one month should be managed with a long-acting angiotensin-converting (ACE) inhibitor and a thiazide diuretic.<sup>2</sup> Until it is proven that the benefit is a class effect, the specific drugs recommended are perindopril with indapamide, according to the PROGRESS<sup>8</sup> trial, or ramipril, according to the HOPE study.<sup>9</sup> The choice of atenolol and enalapril in this patient preceded the publication of the RCP guidelines. Given the regimen selected, the

increased dose of atenolol may give cause for concern. Atenolol lowers raised systolic and diastolic blood pressures by about 15–20 per cent, with the full effect being established in one to two weeks. A dose of 50mg once a day is effective in most patients and dose-response studies have shown no significant difference in antihypertensive effect when the 50mg, 100mg and 200mg doses were compared.<sup>10</sup> The British National Formulary<sup>11</sup> states that blood pressure control can usually be achieved with a 50mg dose, and an increase to 100mg daily is not normally required. Postural hypotension is not common with atenolol, but the other concern is that the dose increase may not achieve the desired therapeutic response.

Blood pressure can be controlled by altering the dose of enalapril, although caution should be exercised if the patient has concomitant aortic stenosis<sup>12</sup> because of the possibility of reduced coronary perfusion. A ward-based pharmacist would be better placed to monitor for therapeutic end points such as appropriate reduction of blood pressure, serum cholesterol and blood glucose, because the full effect will take a few weeks and because long-term control is important. The ward pharmacist should also be involved in implementing the new treatment guidelines.<sup>2</sup> The action required by the dispensary-based pharmacist is therefore to alert the ward-based pharmacist to the potential problem with the drug selection in this setting and the possible inappropriateness of the dose of atenolol.

Aspirin is used to lower the risk of serious vascular events and to reduce the frequency of attacks.<sup>4</sup> Platelet aggregation is a key factor in the formation of atheromatous clots and aspirin is therefore widely used to prevent further TIAs. The antiplatelet effect of aspirin primarily involves the irreversible inactivation of platelet cyclooxygenase, causing decreased platelet aggregation, prevention of release of vasoactive substances and prolonged bleeding time.<sup>7</sup>

In the UK, dosage guidelines differ according to the timing of patient admission with respect to the onset of symptoms. For the acute management of stroke/TIA, the aspirin dose is 160–300mg daily as long as a diagnosis of haemorrhage has been excluded.<sup>2</sup> However, a dose of 75–325mg daily is recommended for secondary prevention<sup>2</sup> in patients first diagnosed with ischaemic stroke or TIA before discharge from hospital or before two weeks have elapsed from the onset of stroke, whichever is sooner. The drug of choice can vary according to contraindications or adverse drug reactions. Clopidogrel, 75mg once daily, or dipyridamole modified-release, 200mg twice daily, are possible alternatives in patients intolerant of aspirin.<sup>2</sup> The North of England Evidence-Based Guideline Development Project's recommendations on the use of aspirin for the secondary prophylaxis of vascular disease in primary care suggests an ongoing dose of 75mg daily for patients with a history of stroke or TIA.<sup>13</sup> The dose prescribed in this patient is 75mg daily. This may be appropriate, depending on when the admission occurred relative to the onset of the disease, and the local policy for patients undergoing carotid endarterectomy. The history of drug-related adverse events and disease control in this individual patient should be considered. The aspirin dose should continue to be used during and after surgery,<sup>14</sup>

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and should be prescribed at discharge as 75mg once daily. The dispensary pharmacist could check the local policy for aspirin dosing with the ward pharmacist.

A competent pharmacist should recognise that this patient is being treated for hypertension and question the dose change of atenolol, bearing in mind its flat dose-response curve. A more experienced pharmacist should be expected to know the recommended anti-hypertensive drug of choice in this common medical condition and be aware of the question relating to the aspirin dose.

## — PRESCRIPTION 2

Figure 5 (p247) shows the solution to prescription 2. This patient was admitted to a neurology ward.

Here, the main pharmaceutical care problem is control of epilepsy in a patient who is not tolerating oral medication. Although again, the underlying problem is not confined to this specialty, the type of patient found on a specialist neurology ward is likely to be more complicated than one found on a general ward. The patient may require a more complicated drug regimen or higher doses to control the epilepsy and close monitoring is required. Carbamazepine and sodium valproate have been prescribed for epilepsy and domperidone has been prescribed for nausea, vomiting, or both.

Carbamazepine is the drug of choice in simple and complex partial seizures, as well as tonic-clonic seizures secondary to a focal discharge.<sup>11</sup> In patients unable to tolerate the oral route of administration, the only option left is to use suppositories, since there is no injectable form. In pharmacokinetic studies, the total bioavailability of carbamazepine from suppositories is about 25 per cent less than from oral formulations,<sup>15</sup> and 100mg orally is equivalent to 125mg rectally.<sup>11</sup> For rectal doses up to 300mg, about 75 per cent of the total drug absorbed reaches the systemic circulation in about six hours.<sup>16</sup> The maximum recommended rectal dose is 250mg four times a day, equivalent to 800mg daily by the oral route<sup>16</sup> because absorption at doses higher than this is unpredictable and non-linear (personal communication, Cephalon). The suppositories are licensed only for short-term use, up to a maximum of seven days, but this is due to the absence of supporting trial data and not because of any known adverse event.

A further complication is that carbamazepine induces liver enzymes, leading to considerable inter-patient half-life variation.<sup>16</sup> Although a steady state serum level is attained in two to four days, it may later decline due to the drug inducing its own metabolism. The drug is usually introduced at a low dose (100–200mg once or twice a day), then increased slowly to the usual dose range of 800mg to 1.2g daily in divided doses.<sup>11</sup> This reduces the risk of side effects such as rash and drowsiness.

In this patient, the oral dose of 500mg twice daily does not easily translate to a rectal dose. The therapeutic plasma range is taken as 4–12µg/ml for the majority of patients.<sup>16</sup> Where suppositories are substituted for tablets, the plasma level reached is generally 5–8µg/ml.<sup>16</sup> Both of these plasma concentration ranges will be subject to inter-patient variation. The pharmacist should probably recommend a rectal dose of 250mg four times a day, but recognise that this may not achieve equivalent serum levels so that close monitoring for control of epilepsy will be required.

The dose and dosage conversion of sodium valproate are both problematic. Sodium valproate can be used in all forms of epilepsy and is available in oral and injectable forms. The BNF recommends that the dose by intravenous infusion for continuation of therapy when the oral route is no longer possible should be the same as the dose by the oral route, since oral absorption is greater than 95 per cent.<sup>11,17</sup> However, the BNF also states that the usual maximum dose in adults by IV infusion and the oral route is 2.5g daily. In patients taking sodium valproate concurrently with other antiepileptics that induce liver enzyme activity, such as carbamazepine, as in this patient, the dosage range may be increased by 5–10mg/kg/day from the usual dosage range of 20–30mg/kg/day.<sup>17</sup> If this patient weighs 75kg,

this would make the total dose of 3g daily correct. The pharmacist should take steps to ensure that the oral dose of 1g three times a day is correct, according to the previous drug history and the patient's body weight. If the oral dose is correct, then the converted IV dose should also be correct. The pharmacist should ensure that an IV monograph detailing administration advice is available, taking particular care to advise the nursing staff if the patient is on a ward where this drug is not used regularly.

Of particular concern could be the reason for nausea and vomiting in this patient. The pharmacist should recognise that, potentially, this is a drug-related adverse effect of both carbamazepine and sodium valproate. Inspection of the drug history and medical notes may reveal whether the onset was related to an increase in dose of either antiepileptic, in which case an initial dosage reduction and more gradual dose titration may be appropriate.

A competent pharmacist should recognise the need to confirm the dose of sodium valproate as a priority, and then check the conversion between different routes of administration. The pharmacist should also demonstrate awareness of the drug-drug interaction and recognise the potential for a drug-related adverse event.

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**Answer sheet (answers are shown in magenta)**

Candidate's name:.....

Prescription number 1

Ward: **Neurosurgery**

Clinical specialty: **Neurology**

Chart endorsements:

Medical problems:

1. Surgery: carotid endarterectomy
2. Transient ischaemic attacks (TIAs)
3. Hypertension
4. Prophylaxis against stroke and myocardial infarction
5. Hypercholesterolaemia
6. Diabetes mellitus, or abnormal blood glucose levels

Pharmaceutical problems:

1. Dose of atenolol in hypertension management in patients with TIA
2. Dose of aspirin in TIAs with respect to onset of symptoms
3. Management of risk of disease progression (monitoring of therapeutic endpoints: blood cholesterol, blood glucose and blood pressure)
4. Choice of antihypertensive in stroke/TIA secondary prophylaxis according to national guidelines
5. Appropriate lifestyle advice, such as smoking cessation, weight reduction and low cholesterol diet

Priority intervention Number 1

Suggested action to resolve the priority intervention:

1. Contact the ward pharmacist to ask for a check on the appropriateness of the choice, and increase in dose of atenolol
2. Request a check of the aspirin dose with respect to management of attacks, previous adverse events and the local policy

Urgency: **Less urgent**

Figure 4: Solution to prescription 1

**Answer sheet (answers are shown in magenta)**

Candidate's name:.....

Prescription number 2

Ward: **Neurology**

Clinical specialty: **Neurology**

Chart endorsements:

Consider administration of intravenous (IV) sodium valproate (unless monograph available on the ward)

Medical problems:

1. Epilepsy
2. Nausea and/or vomiting
3. Inability to tolerate oral medication

Pharmaceutical problems:

1. Dose of sodium valproate
2. Oral to IV conversion of sodium valproate
3. Oral to rectal conversion of carbamazepine
4. Drug interaction between sodium valproate and carbamazepine
5. Possible drug-related event: nausea and vomiting possibly due to sodium valproate or carbamazepine

Priority intervention Number 1, but must mention 2 and 3

Suggested action to resolve the priority intervention:

1. Confirm the drug history to ensure that the 3g daily dose of sodium valproate is correct, and also that there was no recent dose increase of sodium valproate and carbamazepine to account for the nausea and vomiting
2. Check the oral to IV conversion of sodium valproate and oral to rectal conversion of carbamazepine
3. Advise doctor depending on the results of investigations

Urgency: **Urgent**

Figure 5: Solution to prescription 2