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Education

Prescribing for older people

What do you need to be aware of when prescribing for elderly people? **Louise E Cotter** and **Una Martin** discuss

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Prescribing is an essential skill in clinical practice, which requires a sound knowledge of the principles of therapeutics. Many factors influence the way the body handles drugs and the effects seen. Age is particularly important.

If you have ever been attached to a medical firm when it is on call for acute admissions you will know how important it is to prescribe drugs safely to elderly people. About 15% of the population in the United Kingdom is older than 65, and the number of elderly people will continue to rise in the 21st century. The prevalences of many diseases are related to age, and several diseases may coexist in the same patient—for example hypertension, osteoarthritis, and prostatic hypertrophy. Prescribing for these and other conditions means that elderly patients consume half of all prescribed items, and their drug regimens are often complex. The use of cardiovascular drugs, diuretics, analgesics, and hypnotics are particularly common in this age group. In addition, elderly people tend to be high consumers of over the counter preparations, including vitamins, analgesics, and herbal remedies, which may interact with prescription drugs. Finally, both long duration and polypharmacy characterise drug treatment in elderly people. For all these reasons elderly patients may be particularly vulnerable to adverse drug reactions.

Adverse drug reactions

Adverse drug reactions are often a consequence of multiple drug prescribing, which leads to drug-drug interactions. There are many mechanisms involved, including inhibition or induction of drug metabolism by the cytochrome P-450 system in the liver. For example, inhibition of cytochrome P-450 isoenzymes by ciprofloxacin may reduce the metabolism of warfarin, leading to a dangerous increase in the prothrombin time.

Another important drug-drug interaction occurs when a pharmacological interaction between two drugs counteracts the intended effect. For example, coadministration of non-steroidal anti-inflammatory drugs and antihypertensives may lead to a reduced hypotensive effect caused by sodium retention induced by the non-steroidal anti-inflammatory drug. There are many other ways

in which polypharmacy might cause adverse drug interactions, and it is important when patients are taking several drugs to check the interaction section of a reference text—for example, see appendix 1 of the *British National Formulary* (BNF). This will help avoid problems with potentially dangerous interactions.

Studies have shown that adverse drug reactions might cause about 3-12% of hospital admissions in elderly patients. Because drug interactions increase the propensity for adverse drug reactions, an important predictor for the risk of adverse drug reactions is the number of drugs taken simultaneously. In addition, some drugs are much more likely to cause problems in older people, particularly cardiovascular drugs, non-steroidal anti-inflammatory drugs, and drugs that act on the central nervous system. It is often difficult to assess the relative benefits and risks of drugs in older patients, not least because clinical trials are often not performed in elderly people, particularly if they are frail.

The need for pharmacovigilance and the use of appropriate monitoring schemes—for example, the yellow card system in the United Kingdom—are essential to identify problems related to drugs in all age groups. All medical students and junior doctors are encouraged to submit reports of all cases of suspected adverse drug reactions. Each time a patient is seen a careful drug history should be taken and checked with the help of the BNF. All unnecessary or potentially harmful drugs should be stopped. It is only by careful and repeated assessment of a patient's need for drugs that we can make a difference.

Ageing and physiological change

Elderly patients may also develop problems with their drugs because of physiological changes related to age that alter the way in which the body handles drugs (pharmacokinetics) and how the body responds to drugs (pharmacodynamics). It is important to note there are no standard rules for prescribing for elderly people. Biological age does not always reflect chronological age, but elderly people face particular problems, which have been described by Sir Bernard Isaacs as the “geriatric giants” (box 1). Some or all of these problems will affect an elderly patient's ability to cope with drugs. A patient with visual impairment may need help to identify his or her tablets correctly; increased sensitivity to the effects of benzodiazepines may increase the risk of dizziness, falls, and blackouts; and postural hypotension may limit the use of antihypertensive agents. In all cases extreme care should be taken when prescribing any agent to an elderly patient. Doctors should start with the lowest dose; often review the need for ongoing drugs; and take seriously any adverse effects that the patient mentions.

Box 1: The geriatric giants

Incontinence

- Diuretics
- Benign prostatic hypertrophy
- Urinary retention (with or without overflow)
- Large urine production (for example, uncontrolled diabetes mellitus, hypercalcaemia)
- Infection
- Decreased mobility

Intellectual impairment

- Susceptible to many common drugs (for example, opioid analgesics, benzodiazepines, antipsychotics, and antiparkinsonian drugs)
- Depression
- Stroke
- Dementia
- Delirium

Instability

- Postural hypotension
- Visual impairment
- Decreased muscle strength
- Hypoglycaemia

Immobility

- Arthritis
- Instability
- Previous falls
- Changes in drug disposition also occur because pharmacokinetics alter with age (box 2). In practice the most important change is caused by the reduction in renal function that occurs in all elderly patients. Estimation of creatinine clearance is helpful in deciding whether a reduction in dose of a new or ongoing medication is necessary. Useful methods at the bedside include the Cockcroft-Gault formula, based on age, weight, sex, and serum creatinine (box 3), or the modification of diet in renal disease, which does not need the patient's weight and takes ethnic group into account.

Box 2: Pharmacokinetic changes with age

Absorption—Gastric pH is higher because of a reduction in acid secretion, a decrease in gastric emptying, and a decrease in gastrointestinal motility. These changes may lead to decreased absorption but not to a clinically meaningful extent.

Distribution—Total body water, proteins, and lean body mass decrease and total body fat increases. The lower body water may cause a reduced volume of distribution for polar drugs (for example, aminoglycosides, digoxin). The increased fat stores may lead to a larger volume of distribution for lipid soluble drugs (for example, phenytoin, diazepam, and flurazepam).

Metabolism—Hepatic oxidative pathways (phase 1) become less effective and may lead to reduced metabolism of drugs such as benzodiazepines. Phase 2 reactions are generally not impaired. Hepatic mass and blood flow are reduced, which may be more important than enzyme activity, and may lead to a reduced metabolism of many drugs in elderly people.

Excretion—The glomerular filtration rate is reduced, and tubular function changes, affecting aminoglycosides, lithium, and digoxin. Drugs and polar drug metabolites are excreted slowly, and patients are more susceptible to the effects of nephrotoxic drugs.

Box 3: The Cockcroft-Gault calculation

The Cockcroft-Gault calculation estimates renal function by estimating the creatinine clearance (CrCl) and therefore residual renal function in patients with chronic renal failure:

Estimated CrCl = (140-age in years) x weight in kg x 1.23 (or 0.85 for women) / (serum creatinine in $\mu\text{mol/l}$)

Creatinine is influenced by intake of dietary protein, muscle mass, and activity. The inclusion of sex, age and weight in the equation attempts to allow for this variation.

Example

A 37 year old man with a creatinine of $82 \mu\text{mol/l}$, weighing 70 kg has an estimated CrCl = 108 (normal renal function). Whereas an 87 year old man with a 50% rise in creatinine to $123 \mu\text{mol/l}$, weighing slightly less at 60 kg has an estimated CrCl = 31.8 (moderate to severe renal impairment).

To bear in mind

Many elderly patients receive multiple drugs for various comorbidities, increasing the risk of drug interactions and adverse events. Age related changes in drug disposition and increased sensitivity to drugs make elderly patients vulnerable to drug accumulation and toxicity. It is essential to assess the need for existing and new drugs in all cases and to review prescriptions

regularly.

When elderly patients are admitted to hospital, a careful drug history should be taken from the patient or the family, and, if necessary, corroborative information gained from the general practitioner. Factors related to the patient, such as cognition, swallowing, vision, manual dexterity, and attitude to taking drugs should not be ignored. This will affect the clinician's decision in all aspects of treatment, from selection of drugs or formulation to the choice of container on discharge from hospital. Experienced elderly care doctors often spend time on each ward round evaluating potential benefits and risk of falls and other adverse events from each drug the patient is taking and stopping unnecessary or potentially harmful agents. It is only by doing this that we will reduce the risk of adverse events related to drugs in our elderly patients.

Case study

An 87 year old man is referred to the medical admissions unit by his general practitioner with a two month history of dizziness, unexplained falls, and headaches. The general practitioner is concerned that the patient is no longer able to care for himself at home. In addition, he has been complaining of recurrent headaches and a painful right eye, accompanied by mild blurring of vision for the past two days. The general practitioner has attributed this to depression and has recently started him taking amitriptyline. His medical history includes a myocardial infarction in 2004 and essential hypertension. His general practitioner describes him as a "bit of a drinker" and he is a lifelong cigarette smoker.

COMMISSION ON HUMAN MEDICINES
 SUSPECTED ADVERSE DRUG REACTIONS

If you suspect that an adverse reaction may be related to a drug, or a combination of drugs, you should complete this Yellow Card or complete a report on the website at www.yellowcard.gov.uk. For emergency reactions visit www.nps.gov.uk (identified by *). Report all suspected reactions including any considered not to be serious. For amputated limbs and orbital trauma report all serious adverse reactions to include: severe and serious and minor adverse reactions in children (under 18 years). You do not have to complete this form if you are a doctor, dentist, nurse, pharmacist or optician, but because your details are not known, see ENF (page 16) in the NPSRA website (www.yellowcard.gov.uk) for additional advice.

PATIENT DETAILS		Patient Initials: _____	Sex: M / F	Weight (if known) (kg): _____	
Age (at time of reaction): _____		Identification (Your Practice / Hospital Ref #): _____			
SUSPECTED DRUG(S)					
Give brand name of drug and batch number if known	Route	Dosage	Date started	Date stopped	Prescribed for
_____	_____	_____	_____	_____	_____
SUSPECTED REACTION(S)					Unusual:
Please describe the reaction(s) and any treatment given:					Recurrent <input type="checkbox"/>
How serious is it? (1-5) _____ This reaction is unexpected _____					Recurring <input type="checkbox"/>
Do you consider the reaction to be serious? * Yes / No					Continuing <input type="checkbox"/>
If yes, please indicate why the reaction is considered to be serious (please tick all that apply)					Other <input type="checkbox"/>
Patient died due to reaction <input type="checkbox"/>	Involved or prolonged hospital hospitalization <input type="checkbox"/>				
Life threatening <input type="checkbox"/>	Involved paralysis or significant disability or incapacity <input type="checkbox"/>				
Unpleasant abnormality <input type="checkbox"/>	Medically significant (please give details) <input type="checkbox"/>				

*This is a serious event to identify the patient or any other circumstances surrounding the report

On examination his right eye is swollen and congested, with a fixed, dilated pupil, and there is visual field loss in the right eye. His blood pressure is 160/94 mm Hg lying and 125/90 mm Hg standing. His pulse rate is 50 beats/min, and an electrocardiogram confirms sinus bradycardia.

The patient has brought his drugs with him; he takes

Perindopril 4 mg a day

Verapamil modified release 120 mg twice a day

Furosemide 40 mg in the morning

Propranolol modified release 160 mg a day

Simvastatin 40 mg at night

Amitriptyline 75 mg daily

Nitrazepam 5 mg at night

Aspirin 75 mg a day

Senna 15 mg at night

What concerns should you have about this man's presentation and treatment?

He is taking many drugs, which may be causing some if not all of his symptoms. For example, the headaches and eye symptoms are likely to be caused by closed angle glaucoma. This can occur when a patient is treated with a tricyclic antidepressant, such as amitriptyline, because of an antimuscarinic effect. In this situation a selective serotonin reuptake inhibitor may be more appropriate because it has fewer adverse antimuscarinic effects.

The patient has also had dizziness and falls and physical examination shows postural hypotension and bradycardia. His treatment may well be responsible for several reasons. Firstly, he is taking several cardiovascular drugs, all of which may cause postural hypotension (verapamil, perindopril, propranolol, and furosemide). This is particularly likely when all these drugs are given together. In addition, when propranolol and verapamil are coadministered they may block the atrioventricular node in the heart, causing profound bradycardia and even heart block; patients may present with dizziness and falls. Tricyclic antidepressants are also associated with postural hypotension and benzodiazepines, such as nitrazepam, cause an increase in falls in elderly people. Both drugs are more likely to cause sedation if taken with alcohol.

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Competing interests

None declared.

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