

Geriatric prescribing



Curriculum Vitae

Dr Leon Derek Regensberg is currently Specialist Physician and Head of the Department of Medicine at Victoria Hospital, Cape Town. He is also Honorary Lecturer (Geriatric Unit) Department of Medicine, University of Cape Town. In 1972 he was awarded the MB ChB (with Honours) at UCT and then served internship at Groote Schuur, and Addington Hospitals. After medical registrar training at Wentworth and Groote Schuur, he obtained geriatric experience at Manor Park Hospital in Bristol, U.K. and studied geriatric medicine in London and Manchester. In 1981 he was elected to MRCP (UK) through the London College and was appointed to his present post. He was promoted to Senior Specialist in 1983. Dr Regensberg is a member of the S A Gerontological Association and the British Geriatrics Society. He is also Honorary National Secretary of the S A Geriatrics Society.

KEYWORDS: Prescriptions, Drug; Drug Interactions; Drug Resistance; Patient Compliance; Health Services for the Aged; Geriatrics; Aged.

Dr Leon Derek Regensberg MB ChB(UCT) MRCP(UK)
Victoria Hospital
Cape Town
8000

Summary

The amount of drug prescribing is increased among elderly patients and is a frequent cause of ill-health and even hospital admission. Factors which contribute to this include multiple pathology and polypharmacy, inappropriate treatment of the normal ageing process and the doctor's inherent urge to prescribe. Several age-related changes in pharmacokinetics and pharmacodynamics are discussed. Knowledge of these changes is important in order to estimate the safe dosage of potentially toxic drugs. A table of suggestions for safe and effective drug treatment for the elderly is outlined.

Much of the drug therapy dished out to elderly patients takes the form of a 'therapeutic salad' and is often entirely inappropriate. Over 80% of old people are on drug therapy¹ compared to 30% of young people. In March 1982 in the UK some 10 million prescriptions were written for elderly patients²

The reasons for this disproportionate drug prescribing are:

- multiple pathology and polypharmacy
- inappropriate treatment of the normal ageing process such as mild elevation of blood pressure and mild glucose intolerance
- 'prescription reflex' — used to deal with talkative patients and the common psycho-social problems of the aged.

Drug interactions and adverse reactions are understandably common in old age for the following reasons:

- Drug trials seldom involve the elderly
- Multiple drugs from different sources are used
- Problems arise with compliance, especially if complex regimens have to be followed.

A. PHARMACOLOGY OF OLD AGE

DRUG EFFECTS

The effect of any drug, as in the young, is dependent on bioavailability and tissue sensitivity. These are modified by the normal ageing process and the presence of multiple degenerative diseases. In addition, drugs have multiple actions, many of which are unwanted. (You don't get something for nothing in life!) The 'elderly' are a heterogeneous group ranging from the 'young' old to the very old, and their ability to handle drugs varies.

ABSORPTION:

Normal changes in old age include:

- hypochlorhydria;
- reduced surface area for absorption (30%);
- reduced blood flow to the gut;
- slower gastric emptying and a longer transit time.

Despite these changes there is little evidence to suggest that drugs are poorly absorbed in the elderly. Hypochlorhydria may prevent enteric coated tablets from being absorbed (eg Slow-K). However, polypharmacy and drug interaction is more important.

Transit time. Maxalon will reduce transit time and may reduce the absorption of digoxin. Anticholinergics will increase transit time and possibly increase absorption of digoxin.

Inhibition of absorption occurs when insoluble complexes are formed, as with iron and tetracycline; antacids and digoxin.

Complex changes occur in pharmacokinetics and pharmacodynamics with ageing.

DISTRIBUTION:

The body composition changes with ageing.

Body fat increases. This results in an increased volume of distribution of lipophilic (fat-soluble) drugs, eg Diazepam, and prolongs their half-life.

Body water decreases. This results in a reduced volume of distribution of water-soluble drugs and may increase their plasma concentration.

Lower plasma albumin. This results in reduced binding sites for highly protein-bound drugs, eg warfarin, epanutin and diazepam. Since the unbound drug is active, more is available to produce an effect. Other drugs may also compete for available binding sites and displace more free drug, further increasing the effect.

Changes in regional blood flow to the liver and kidneys reduce perfusion.

Increased permeability of the blood-brain barrier

This may be important with respect to effect of psychotropic drugs.

METABOLISM:

Metabolism mainly takes place in the liver. The changes which occur with ageing are:

- the number of hepatocytes falls
- they atrophy and vary in size,

- there is a fall in albumin synthesis,
- hepatic blood flow is decreased (1400 ml/min to 800ml/min.)

The object of liver metabolism is to convert lipid-soluble drugs into water-soluble compounds which can be excreted by the kidneys.

Drug trials seldom involve the elderly.

Phase I: Oxidation/Reduction by microsomal cytochrome P450 system.

Phase II: Conjugation reactions — glucuronidation — acetylation

N.B.: Phase I metabolism is thought to be impaired in the elderly, Phase II metabolism is unchanged. Therefore drugs requiring phase I metabolism (eg Librium), will have a longer action than drugs requiring only phase II metabolism (eg Ativan). The short half-life is thus retained. Cimetidine may block phase I metabolism further.

Slow hepatic metabolism is probably multifactorial:

- The nutritional state is often poor in elderly patients.
- Liver disease such as cirrhosis further reduces hepatic blood flow.
- The use of other drugs may damage the liver (eg alcohol), it may cause enzyme induction (eg barbiturates), and may block phase I metabolism (eg cimetidine).
- The normal ageing process impairs phase I metabolism and hepatic blood flow is reduced.
- Smoking is an enzyme inducer which can be less significant in the elderly because the enzymes are working at maximum capacity already!

'First-pass' extraction of orally administered drugs may be reduced. Drugs which are normally highly extracted from the portal blood include propranolol and oral morphine, hence the difference between an oral and an IV dose. Higher than normal plasma levels may result, although the half-life remains normal. Intra-venous administration of the same drugs results in a prolonged half-life, probably because of impaired hepatic blood flow?

With ageing the most consistent change is the decline in renal function.

EXCRETION

A normal predictable decline occurs in renal function with ageing. Glomerular filtration rate (GFR) and renal blood flow fall by 40-50% by the age of eighty. This may be compounded by dehydration, hypotension and cardiac failure. Serum Creatinine is often normal, due to reduced muscle bulk, but it is essential to do creatinine clearance to measure renal function. There is reduced excretion of many drugs. Most important are those with a narrow therapeutic index where the difference between the toxic level and therapeutic level is small: digoxin and aminoglycoside antibiotics. Nomograms are available, but as a rule of thumb it is best to assume a 50% reduction in renal function and to reduce the dose accordingly. Blood levels are useful if available.

ALTERED TISSUE SENSITIVITY:

There is an increased sensitivity to certain benzodiazepines, eg Nitrazepam, which is well described by Castleden³ and Reidenberg⁴. This may be due to altered permeability of the blood-brain barrier, however. There is also an increase in effective analgesia with morphine⁵, but one must remember the pain threshold is raised in the elderly. Furthermore, there is

About 10% of geriatric patients are admitted to hospital solely because of adverse reactions to drugs.

an increased sensitivity to warfarin despite lower doses⁶ and possibly to digoxin as well. There seems to be a *decrease* in sensitivity to propranolol with fewer side-effects (anecdotal) despite higher average blood levels (reduced first-pass extraction). Some evidence also suggests that there is an age-associated reduction in the number of beta-adrenergic receptors within the ageing cardiovascular system.⁷

IN SUMMARY

Complex changes occur in pharmacokinetics and pharmacodynamics with ageing, which are not yet fully worked out. Extra caution is needed with a variety of drugs. For example, Diazepam which is lipid-soluble (so increased half-life); undergoes phase I metabolism, and is highly protein bound with possible increased tissue sensitivity. It is hardly surprising, therefore, that over-sedation is common. The most *consistent* change is the decline in renal function with ageing.

B. SPECIAL PROBLEMS IN GERIATRIC PRESCRIBING

These are adverse reactions, unintentional polypharmacy and non-compliance.

ADVERSE REACTIONS

Adverse reactions are the result of enthusiastic polypharmacy and altered handling. About 10% of geriatric patients are admitted to hospital solely because of adverse reactions to drugs.⁸ The commonest offenders were: sedatives, diuretics, anti-hypertensives and digoxin. It was also observed that the ability to recover from these reactions was impaired. Adding another drug was **not** the best treatment! The incidence of adverse reactions is even higher among in-patients,^{9, 10} probably because non-compliance is eliminated. Some common adverse reactions are:

Neuropsychiatric syndromes — Confusion (digoxin, sedatives, anticholinergics).

- Agitation (benzodiazepines)
- Dementia (N.S.A.I.D.)
- Depression (reserpine, methyl dopa)
- Parkinsonism (phenothiazines)

Anticholinergic effects

- Glaucoma
- Urinary retention
- Constipation (anti-depressants, Benzhexol)

Hypotension — "Dizziness" and Falls (diuretics, sedatives)

Others

- Dehydration/Electrolyte disturbances (diuretics)
- Gout (thiazide diuretics)
- Hyperglycaemia (thiazide diuretics, steroids)
- Angina (thyroxine)

UNINTENTIONAL POLYPHARMACY

This is caused by the use of 'over-the-counter' drugs (analgesics, cough remedies, etc); alcohol (often part of a patent remedy); pill swapping and hospital hopping (and drug collecting).

NON-COMPLIANCE

This may be beneficial! It is probably not much different in the young, although it tends to be more often accidental in the elderly, rather than deliberate. During one investigation in Glasgow, 2¼ tons of drugs were returned!

CAUSES OF NON-COMPLIANCE

- Inadequate patient instruction/education
- Mental disability (poor memory, confusion, apathy)
- Physical disability (poor sight, loss of manual dexterity)
- Polypharmacy or complex regimens
- Cost

Compliance may be improved by giving patients a chart on which all the drugs and the times at which they should be taken are recorded.

There is the temptation to treat every new complaint with a drug.

SOME COMMONLY USED DRUGS

Digoxin — Some 5% of elderly population use digoxin regularly and most can be stopped.¹² Confusion is an early sign of toxicity. There could be an increased sensitivity, so use of levels to exclude toxicity.

Diuretics — Salt and volume depletion occur and may produce hypo- or hyperkalaemia, gout and glucose intolerance. Diuretics are often over-prescribed in combination therapy (Rautrax).

Anti-hypertensives — These may be unnecessary in very old. Side-effects may out-weigh advantages. Beta-blockers are well tolerated. 'Non-drug' treatment is important to consider: low salt diet, weight loss, no smoking and exercise.

Anti-depressants — Side-effects are common, but are often useful drugs.

Sedatives — Benzodiazepines can cause paradoxical excitement or over-sedation.

Hypnotics — Avoid long-acting drugs (nitrazepam) and continuous use.

Analgesics — Consider increased sensitivity post-op.

NSAID — Side-effects are similar to young patients, dementia and fluid retention also occur. Avoid long-term use as renal damage is increased.

Anti-diabetic agents

- Biguanides — Use in obese patients only and keep the problem of lactate acidosis in mind.
- Sulphonylureas — avoid long acting drugs like chlorpropamide.
- Diet controls most maturity-onset diabetics.

SUGGESTIONS FOR SAFE AND EFFECTIVE DRUG THERAPY IN THE ELDERLY

1. Avoid treating symptoms and withdraw unnecessary medication ('Reverse prescribing').
2. Establish if the patient needs drug therapy at all.
3. Reduce dosage — small initial dose and titrate response and use drugs with a short half-life.

Geriatric prescribing

4. Use as few drugs as possible, as seldom as possible, preferably linked to a familiar activity.
5. Review long term therapy frequently (eg digoxin, sedatives, diuretic).
6. Use an easily self-administered dosage form.
7. Use suitable containers with clear labelling.
8. Educate the patient or a responsible relative about the drug, possible side-effects and drugs to avoid (eg alcohol).
9. Check that the patient is not receiving drugs from another source.
10. Establishment by appropriate trials that drugs are safe for use by the elderly (ie better education of the pharmaceutical trade).

CONCLUSIONS

Prescribing drugs is a kind of ritual with a significance of its own apart from the obvious pharmacological aspect, and it is often easier to add another drug than to delete one. There is a temptation to treat every new complaint with a drug, but it should be realized that illness may be caused by drug therapy. One should not withhold drugs from the elderly on the grounds of age alone, provided that they are indicated, but one should be aware that polypharmacy and unnecessary drug therapy can cause more harm than good and adversely affect the quality of life in old age. Conservative prescribing and a knowledge of the altered action of drugs in old age will contribute to safe and effective drug therapy for the elderly.

References:

1. Knox JDE. Prescribing for the elderly in general practice. A review of current literature. *J R Coll Gen Pract* 1980; 30(suppl 1).
2. Castledan CM, George CF. The effect of ageing on the hepatic clearance of propranolol. *Br J Clin Pharmacol* 1979; 7: 49-54.
3. Castledan CM, George CF, Marcer D, Hallett C. Increased sensitivity to nitrazepam in old age. *Br Med J* 1977; 1:10-2.
4. Reidenberg MM, Levy M, Warner H et al. Relationship between diazepam dose, plasma level, age and central nervous system depression. *Clin Pharmacol Ther* 1978; 23:371-4.
5. Bellville JW, Forrest WH, Miller E, Brown BW. Influence of age on pain relief from analgesics. A study of postoperative patients. *JAMA* 1971; 217:1835-41.
6. O'Malley K, Stevenson IH, Ward CA, Wood AJJ, Crooks J. Determinants of Anticoagulant control in patients receiving warfarin. *Br J Clin Pharmacol* 1977; 4:309-14.
7. Schocken, DD, Roth GS. Reduced β -adrenergic receptor concentrations in ageing man. *Nature* 1977; 267:856-58.
8. Williamson J, Chopin JM. Adverse reactions to prescribed drugs in the elderly — a multicentre investigation. *Age and Ageing* 1980; 9:73-80.
9. Hurwitz N. Predisposing factors in adverse reactions to drugs. *Br Med J* 1969; 1:536-39.
10. Seidl LG, Thornton GF, Smith JW, Cluff LE. Study on the epidemiology of adverse drug reactions III. Reactions in patients on a general medical service. *Bull Johns Hopkins Hosp* 1966; 119-299.
11. Caird FL. Metabolism of Digoxin in relation to therapy in the elderly. *Gerontol Clin* 1974; 16:68-74.
12. Dall JLC. Maintenance digoxin in elderly patients. *Br Med J* 1970; 2:705-6.

STOPAYNE 55 TABLETS:
Reg. No. (Act 101/1965)
Paracetamol 320 mg,
Codeine phosphate 8 mg,
Caffeine alkaloid 32 mg,
Meprobamate 150 mg.
CAPSULES:
Reg. No. C/2.9/15
(Act 101/1965)
Paracetamol 320 mg,
Codeine phosphate 8 mg,
Caffeine alkaloid 48 mg,
Meprobamate 150 mg.

The signs and symptoms are

reduced mobility ●
stiffness ● PAIN ●
tenderness and
joint enlargement

Rx For pain
Stopayne.

One
name
that
stops
pain



Osteo-arthrosis