Drugs for the Elderly
Second edition
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Drugs for the elderly
Second edition

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Drugs for the elderly
Second edition
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In 1984 the World Health Organization (WHO) "parliament", the World Health Assembly, discussed ways of promoting rational use of drugs. There was concern about the high proportion of health budgets spent on drugs in many countries. Such excessive expenditure, in times of economic constraint, limits the funds available for improving primary health care and for ensuring adequate health care to the whole population, young and old alike. Patterns of drug prescribing for the elderly, as reported by a WHO Technical Group, show that half of the total drug consumption is by people aged 60 years and over in those countries where the proportion of this age group is very high (about 20%). The same Group made a review of drug consumption and found that the mean number of drugs being prescribed at any one time was 3.2 per individual in the community in Canada, 4.6 per patient in hospital in Scotland and 8 per person in long-term care in an institution in the United States. While many of these drugs help improve the survival and quality of life of elderly people, the WHO Group pointed out that one fifth of patients entering the geriatric department of a general hospital have symptoms that are attributable to the effect of prescribed drugs. The aim of this book is therefore to promote drug use in the elderly that is efficacious and safe.

One way to ensure the appropriate use of prescription drugs is through the training of health personnel. It is hoped therefore that this book will find its way on to the library shelves of medical, pharmacy and nursing schools around the world. This global dissemination of information is a task entrusted to WHO in a World Health Assembly resolution on the rational use of drugs (WHA37.33), which requests the Director-General "to continue to develop activities at national, regional and global levels aiming at the improvement of ... prescription practices and the provision of unbiased and complete information about drugs to the
health profession and the public". This task was subsequently reiterated in WHA resolutions WHA47.13 and WHA49.14.

WHO set about obtaining unbiased and complete information for the first edition of this book, which was published by the Regional Office in 1985. Contributions were written by experts, and these were then reviewed by an international editorial board. The present edition is an update of this work, with additional authoritative information from the recent international scientific literature. Relevant sources of this additional information are mentioned in an annex to the book. I should like to thank both the original contributors and the reviewers for undertaking this task, as requested by the WHO Member States.

J.E. Asvall
WHO Regional Director
for Europe
Introduction to the first edition

The purpose of this monograph is to describe the principles of drug treatment in old age and the best therapeutic practice for the elderly. It is not a textbook of geriatric medicine, in which far more is involved than drugs.

In the treatment of elderly people, many variations are necessary from “standard” recognized therapy. This is due both to aging itself and to common age-related diseases. Without a proper appreciation and knowledge of them, prescribers will place elderly patients at serious risk of harmful drug effects or (if patients are not given the therapy they need) will deny them the many advantages of correctly conducted treatment. The objective should always be safe and efficacious therapy.

Those aspects of therapeutics that raise no particular problem in the elderly have been deliberately omitted or dealt with very briefly, as have the specialized subjects of drugs used in anaesthetics, in diagnostic procedures (e.g. radiology) and nuclear medicine, and in cancer therapy. We have not considered traditional and herbal remedies, because there is in most cases no scientific evidence of their efficacy.

Some modifications have been necessitated by national variations in practice. In addition it has been necessary to bear in mind that the availability of some drugs varies in different parts of the world. The present text is based on those drugs likely to be available in most countries and thus of universal relevance. The drug monographs are grouped according to the anatomical therapeutic chemical (ATC) classification system developed by the Nordic Council on Medicines and recommended by WHO for use in drug utilization studies.

F.I. Caird, Editor-in-Chief
Glasgow, 1984
Introduction to the second edition

When the WHO Regional Office for Europe launched the first edition of *Drugs for the elderly* ten years ago, it was an immediate success. French and later Russian editions ensued. The book was reprinted twice and, because demand persisted, a further reprinting was considered. During that time, however, remarkable progress had been made in clinical pharmacology and pharmacotherapy. In particular, the aging of the world’s population has stimulated interest in the use and misuse of drugs in the elderly. More than 20 authoritative textbooks have been published since the first appeared in 1979, and scores of articles and reviews are now available. Most of this information is either out of reach of the poorer countries, however, or is far too expensive to obtain. For that reason there still seemed to be a niche for a small, internationally available and understandable, and relatively inexpensive book on the subject. Since medical practice as such has not undergone very drastic changes, the main body of the text has been left untouched, but fundamental changes have been introduced throughout in the views on drug therapy and the choice of available drugs. As time and funds were short, it was impossible to repeat the original approach taken – multi-authorship and an editorial committee of international experts. Revision was mainly done within and later outside the Regional Office with the help of available books and databases. I am very grateful to Dr Hans Liedholm and Ms Agneta Björck Linné (Department of Community Medicine, Malmö University Hospital, Sweden) for reviewing the final version of the manuscript and suggesting a number of useful changes and additions.

Because of the anticipated wide distribution of this book in the WHO European Region, and especially in the countries of
central and eastern Europe and the newly independent states of the former USSR, drugs on the WHO Model List of Essential Drugs have been given some preference over others.

In the first edition references to the literature were deliberately omitted. Inserting references throughout the text of this edition would have made the book unwieldy, too large and too expensive. The main sources of information and suggestions for further reading are therefore given in Annex 1. Care has been taken that all recommendations are supported by appropriate data from the literature. Although the Editor of this revision takes full responsibility for any remaining scientific errors, WHO cannot be held liable for either the choice of drugs or recommendations on dosages.

L. Offerhaus
Copenhagen, 1995
The problems of drug therapy in the elderly

Problems with drug therapy in the elderly are numerous and drugs often interact in complicated ways. Their causes and how to deal with them are described in detail in later sections but they may be set out under three headings:

the patient

the prescriber

the drugs

The patient

The main problems from the point of view of the patient may be defined as follows.

Multiple pathology in elderly patients tends to lead to their consuming more drugs than younger patients, with the result that they run a greater risk of developing adverse side effects and drug interactions.

Failure to comply with a drug regimen and errors in administration increase with age. This derives in part from confusion resulting from multiple drug therapy; a bad memory, failing vision and impaired manual dexterity are also important factors. Poor packaging of drugs makes compliance more difficult than it need be. But the most important cause of poor compliance is that patients and their families may fail to understand what they are supposed to do.
Exceptions to normal patterns of drug kinetics and dynamics occur more frequently in old people than in a younger population.

Loss of reserve functional capacity of the heart, liver and kidneys and deterioration of homeostatic control add to the increased vulnerability of old people to drugs.

In old people the outcome of therapy is more likely to be affected by the simultaneous use of old or borrowed drugs, or self-medication with over-the-counter products.

The prescriber

The principal problem affecting prescribers is that inadequate teaching often leads to ignorance about the many differences between old people and younger people with respect to drug therapy. Part of this ignorance is genuine in the sense that much is not understood, but much is in fact known and not properly applied. Prescribing is always the responsibility of the prescribers and they will best protect themselves by adequate knowledge.

Multiple pathology is so common in the elderly that difficult decisions have to be taken about which condition should be treated first and which should be, perhaps temporarily, left untreated, i.e. an order of priorities must be established. There may also be no drug available for some conditions, and therefore it must be accepted that not all conditions found can be treated with medicines (see Table 1). Multiple pathology is a standing invitation to multiple prescribing, and the problems this raises will be even greater if drugs are given to treat the side effects of other drugs. Simplicity is the most important single principle for prescribers to observe.
Table 1. Drugs of uncertain or no value in the elderly

| Drugs claimed to counter mental or physical senility |
| Drugs with purported aphrodisiac properties |
| Peripheral and cerebral vasodilators |
| Expectorants |
| Analeptics |
| Anti-obesity drugs |

The drugs

Particular problems with the drugs themselves that arise in old age include:

- alterations in drug kinetics
- alterations in drug dynamics
- interactions between drugs (more common the more drugs are taken)
- the physiological effects of aging and disease.

Because of such uncertainties, one should generally be cautious of using new drugs in the elderly.
Some of these problems are discussed in more detail in later sections.
How aging may affect drug action

A rational approach to drug therapy in the elderly requires an understanding of the changes in pharmacodynamics (drug response) and pharmacokinetics (drug handling) that are likely to occur in this age group. The two are essentially interrelated since pharmacodynamics, which may in a general sense be determined by the amount of active drug available at the site of action (be it a physiological function or a pathological process), will obviously be influenced by pharmacokinetic changes in the elderly. Alterations in the sensitivity or density of the receptors on which drugs act or in the integrity of the physiological homeostatic mechanisms are further factors that, together with the presence of disease, are likely to influence pharmacodynamics in old age.

As yet it is not possible to separate clearly age effects *per se* from those resulting from aging associated with the presence of disease. It is therefore important to appreciate the large variability in drug response that occurs in a heterogeneous elderly population, ranging from “fit old folk” to the grossly debilitated. The presence of multiple pathology and the consequent need in many cases to prescribe several drugs concurrently adds a further complication. The consequences of alterations in pharmacokinetics or drug sensitivity in the elderly will obviously be more important with those drugs that have a narrow safety margin, such as cardiac glycosides and anticonvulsants.

**Pharmacokinetics**

Pharmacokinetics may conveniently be considered under the headings of absorption, distribution, hepatic metabolism (including presystemic elimination, i.e. rapid intestinal or hepatic inactivation before the drug reaches the systemic circulation) and renal excretion.
With old age a number of changes occur in the gastrointestinal tract that might be expected to alter drug absorption, for example increased gastric pH, decreased intestinal blood flow secondary to decreased cardiac output, and alterations in gastric emptying time and gastrointestinal motility. It is perhaps surprising therefore that, with some notable exceptions such as phenytoin, barbiturates and prazosin, the available evidence indicates that the rate and extent of drug absorption are unchanged in the elderly and that changes, where they do occur, are unlikely to be of clinical significance, particularly during long-term therapy. The increased bioavailability of levodopa and propranolol in some elderly patients results in part from decreased inactivation in the gastrointestinal tract. In the case of levodopa this may influence the therapeutic outcome, at least when the drug is not given together with a decarboxylase inhibitor.

The most important features of a drug's distribution relate to that in the body fluids and the extent of binding to plasma proteins (usually to albumin but, with some drugs, to other proteins such as α, acid glycoprotein), to red cells and to body tissues, including the target organ. In old age there is a significant decrease in lean body mass and total body water, an increase in body fat (particularly in males) and a small but significant decrease in plasma albumin. While it is difficult to generalize, the distribution volume of water-soluble drugs such as furosemide and paracetamol may decrease in the elderly, while lipid-soluble drugs such as lidocaine, amitriptyline and diazepam appear to be more extensively distributed. Overall, the elderly are smaller in body size than younger people and this may contribute in part, for example, to the higher blood levels of digoxin in the elderly than in the young following the same intravenous dose. The age-related decrease in plasma albumin concentration, which is slight in healthy old people, may be more significant in ill, poorly nourished or severely debilitated old people and will result in an increase in the free, pharmacologically active fraction of some drugs, sometimes
leading to more marked effects but more rapid elimination. The practical significance of such changes in distribution volume and extent of protein binding is unclear, but they are of major importance in the interpretation of other pharmacokinetic data, such as the plasma half-life of drugs. It is doubtful whether changes in protein binding in healthy old people are of clinical importance, although the possibility of such changes influencing, or reflecting an alteration in, a drug’s penetration to its site of action cannot be excluded. There is as yet a shortage of information on this, even from animal studies, and it should be realized that subtle changes in drug distribution in the elderly may occur in the absence of any significant alteration in plasma pharmacokinetics.

The onset of drug effect is largely determined by the rate of absorption and manner of distribution. The duration of effect is influenced more by the rate of elimination, principally by metabolic degradation in the liver, usually to more polar, less active metabolites or by renal excretion of the parent drug or its metabolites. The hepatic clearance of phenazone (antipyrine), a drug widely used as an index of liver microsomal oxidation, is reduced in the elderly, partly due to an age-related decrease in functional liver volume and partly to a reduced rate of hepatic metabolism. Several other drugs undergoing oxidation exhibit a similar reduction in clearance (e.g. chlordiazepoxide, theophylline) but for some other drugs (e.g. warfarin, diazepam) no age-related differences in clearance exist. It is apparent therefore that there is no simple pattern of age-related change in drug metabolism. Changes, where they occur, are often small and may be less important than those brought about by environmental factors such as cigarette smoking.

A number of drugs are so avidly extracted by the liver, i.e. by uptake into hepatic binding sites and by metabolism, that their clearance depends on the rate of delivery to the liver by the blood. In old age a decrease in hepatic blood flow, together with a possible reduction in the rate of hepatic metabolism, is responsible for the reduced elimination of such high-clearance
drugs as labetalol, lidocaine and propranolol. With such highly cleared drugs there is a marked first-pass effect due to their extensive presystemic removal from the blood on their first passage through the liver. Their oral bioavailability is therefore low but is increased in the elderly due to a reduction in the first-pass extraction.

Drug metabolizing ability may be enhanced by treatment with enzyme-inducing agents such as phenobarbital or phenytoin, or by exposure to environmental factors such as cigarette smoking. There is limited evidence to suggest that the induction response may be reduced in the elderly. If this is the case, the elderly, as well as having a lower baseline ability to metabolize some drugs (e.g. rifampicin, disopyramide) will be less able to develop tolerance to metabolized drugs.

The effects of age on renal function exert a profound influence on the elimination of a number of drugs. In many cases drugs are excreted by simple glomerular filtration, and their rate of excretion correlates with the glomerular filtration rate (and hence with creatinine clearance), for example digoxin and the aminoglycoside antibiotics. In old age renal function diminishes, together with renal blood flow, so that by the age of 65 there is a reduction of approximately 30% in the glomerular filtration rate compared with young adults. The range is wide, however, and many elderly people maintain a perfectly normal glomerular function. Tubular function also deteriorates with age, and drugs such as penicillin and lithium, which are actively secreted by the renal tubules, show a marked reduction in clearance. In addition to physiological decline in glomerular and tubular filtration, the elderly patient is particularly liable to renal impairment due to dehydration, congestive heart failure, hypotension and urinary retention or to intrinsic renal pathology such as diabetic nephropathy or pyelonephritis, which may further modify the renal handling of drugs.

Where there is obvious renal disease, guidance on the appropriate dosage of renally excreted drugs may be obtained from standard tables. Because of diminished muscle mass and lower
protein breakdown, apparently normal blood urea or creatinine values do not preclude a substantial deterioration of kidney function; the renal reserve is smaller in elderly patients than in younger people and therefore the dose of such drugs should always be chosen with this in mind. This is particularly important because of the serious effects of overdosage with some drugs, for example digoxin, lithium and aminoglycoside antibiotics. In general, elderly patients are best treated with lower doses of renally excreted drugs than are younger patients.

Much of the pharmacokinetic data on hepatic metabolism and the renal excretion of drugs in the elderly has been obtained from single-dose studies, and there is a lack of data on age-related comparisons of steady-state drug levels with long-term dosing. With renally excreted drugs such as digoxin, lithium, penicillin and streptomycin, adequate serum levels are obtained in the elderly with lower doses. With metabolized drugs it is again not possible to generalize. Plasma steady-state levels of propranolol and phenytoin increase with age as do those of some, but not all, tricyclic antidepressants.

Receptor sensitivity

Although pharmacokinetic differences can account for many age-related alterations in drug effect, there is still a significant residue of altered responsiveness that seems to be explicable only by a change in tissue sensitivity to drugs. This age-dependent difference in responsiveness is so great with some drugs that the effect may differ from the usual pharmacological spectrum of the drug in question.

Practical and methodological difficulties preclude in almost all cases the true determination of numbers and sensitivity of receptors and, for the most part, the data available simply relate the plasma drug concentration to the pharmacological effect. Using this approach, the elderly central nervous system shows an increased sensitivity to single doses of psychotropic drugs such as morphine, almost all benzodiazepines and most
antipsychotics. Such age-related changes do not result from altered pharmacokinetics, although the possibility of an increased penetration of the drugs into the elderly brain cannot be ruled out. Increased sensitivity to drugs can occur in other systems; for example, coumarin anticoagulants have a greater effect on clotting factor synthesis in the elderly in the absence of changed pharmacokinetics.

The only receptor system for which any appreciable data exist in relation to human aging is the beta-adrenoreceptor. Evidence from studies on the blockade by propranolol of either isoprenaline-induced or exercise-induced tachycardia indicates that both drugs have a reduced effect in the elderly. This would seem from studies on human lymphocytes to be related to a reduction in the number of such receptors or to an alteration in their characteristics in old age.

**Drug interactions**

Drug interactions stemming from effects on pharmacokinetics, thus altering the amount of drug reaching receptor sites, or from modification of the events at the receptor occur in all age groups. The frequency of their occurrence, however, is directly related to the number of drugs prescribed and for this reason such polypharmacy is particularly hazardous in older patients. In addition this frequently leads to admission to hospital.

**Homeostatic mechanisms**

Reduction in the efficiency of the homeostatic mechanisms appears to be an integral part of the aging process, with the result that the elderly are less able to compensate for the effects of many drugs and are therefore more vulnerable to their adverse effects.

As a result of impaired baroreceptor function, drug-induced postural hypotension is particularly evident in the elderly. Drugs used in the treatment of hypertension are prominent offenders;
in particular, the thiazide diuretics carry a high risk of postural hypotension, as do a number of psychotropic agents such as the phenothiazines, tricyclic antidepressants, monoamine oxidase inhibitors and antihistamines.

The elderly have a marked reduction in their ability to thermoregulate, and drug-induced hypothermia, resulting from a direct pharmacological effect or indirectly through reduced mobility, is a particular problem associated with old age. The phenothiazines produce particular difficulties in this respect, but barbiturates, benzodiazepines, tricyclic antidepressants, narcotic analgesics and alcohol, alone or in combination with other drugs, may also produce considerable difficulties.

Falls occur frequently in old age as a result of impaired maintenance of posture, and drug-induced increases in the frequency of falls may well result from the effects of drugs on the mechanisms of postural control. Such sudden falls may also be caused by drug-induced arrhythmias. For this reason anti-arrhythmic drugs should be reserved for the treatment of life-threatening arrhythmias.

The maintenance of normal intellectual function, the regulation of blood sugar levels and the neurological control of bladder and bowel function may also be less efficient in old age, leading to increased sensitivity to the pharmacological or adverse effects of a variety of drugs.

Pathology

There are considerable difficulties in attributing age-related alterations in drug response to age per se or to age associated with pathological change, and exact comparability of groups is essential in such comparisons. Elderly patients often have multiple pathology, and marked alterations in pharmacodynamics and pharmacokinetics may occur, stemming either directly from the pathology or indirectly from associated complications such as poor nutrition, anaemia, and failure of the hepatic, renal, cardiac or peripheral circulation. The increased risk of haemorrhagic
complications of anticoagulants in the elderly is due, at least in part, to degenerative vascular disease diminishing the haemostatic response. Fortunately knowledge of the effects of disease on drug effects in the elderly is now rapidly improving, and research in this field is expanding.
Choosing the right preparation

Some old people may have difficulty in getting to a pharmacy, perhaps because of distance or infirmity. It is little use prescribing a drug if the prescription is not going to be filled. Sometimes the pharmacy does not stock a particular drug, and it will be useful to ascertain the availability beforehand.

**Oral preparations**

**Containers**

Many old people are alert and have clear vision and nimble fingers. They experience no greater difficulty in taking drugs than their younger counterparts. At the opposite end of the spectrum are patients with mental impairment, poor vision, swallowing problems and arthritic hands. Here many obstacles lie between the drug in its container and the target organ in the patient.

Old people often have difficulty in getting drugs out of containers. Medicine bottles should therefore be large enough to be easily handled, have a neck through which tablets and capsules easily flow, and have a top that is easily removed (or replaced) by screw or bayonet action.

Containers in current use often have childproof lids; one old person in ten cannot open these. A much larger proportion can use the container, but experience such difficulty that compliance is seriously reduced. Most patients solve the problem by not closing the lid after use. Childproof containers, then, should be issued to old people only when they are living with young children. In such a case the pharmacist should ensure that either the patient or a relative knows how to operate the container.
Tablets and capsules in bubble packs should not be dispensed to old people; about a third of them do not have the manual dexterity to open these packs. An even greater proportion either crush the tablets or drop them on the floor when using bubble packs.

Attempts have been made to improve compliance by placing drugs in dispensers with compartments labelled with dates and times. These are rarely successful with old people, who often cannot get their fingers into the compartments or turn the dispenser upside down so that all the tablets fall out. Bubble packs labelled with dates and times have also been prepared for individual patients; if patients understand their use, these can occasionally be quite practical.

Cost

The prescriber should consider the cost of the course of treatment, especially where elderly patients will have to pay for the drugs themselves.

Information

Containers should be labelled with lettering clear enough to be seen by patients with failing vision. Important information comprises the names of the prescriber and patient, the name of the drug, the method and frequency of dosage, and the condition for which it is prescribed. Vague instructions such as "as directed" should be avoided. The label should also give the name of the pharmacist, the date of dispensing and the date of expiry. Such information reduces the risk of one spouse taking the other's tablets, or an old person hoarding a medicine and using it long after expiry of its shelf life. About 25% of elderly patients are not able to remember what the purpose of the drug was.

Tablets and capsules are more easily identified if they are in a container made from clear glass. Dark glass should be used only if light is likely to have a serious effect on the stability of the preparation.
Doctors and pharmacists should also ensure that, after a patient has been discharged from hospital, the local pharmacist dispenses tablets with the same size, shape and colour as those used previously. The patient will also be confused if the name of the drug is changed from a generic to a proprietary one or vice versa. Such confusion is often difficult to avoid when the patient is moved from home to hospital or vice versa. The increasing use of generic drugs and the avoidance of colouring matter often lead to the pharmacist's handing out round white tablets of almost uniform size, and this may bewilder many old people.

Size, shape, colour and appearance of tablets and capsules

Old people have difficulty in swallowing large tablets, particularly if they have a dry mouth or a bulbar or pseudobulbar palsy. Conversely, patients with poor eyesight or arthritic hands may have difficulty in coping with small tablets. Each patient, then, requires individual assessment. In addition to not working, an unchewed tablet may cause local irritation; old aspirin tablets, for example, may cause unpleasant mouth ulcers in old people.

Consideration should also be given to the rate at which tablets travel down the oesophagus. Abnormal motility patterns may lead to considerable delay in old people. The dissolving of irritant tablets in the oesophagus accounts in part for the high incidence of gastrointestinal disturbances associated with medication in the elderly. Drugs causing this include doxycycline, non-steroidal anti-inflammatory agents (including aspirin), iron salts and some anticholinergic drugs. General rules for reducing the problem are that tablets will move more rapidly if they are small, of high density and oval rather than round. Again, tablets are less prone to stick than capsules, and should be prescribed in preference if there is a choice. Rapid transit is also more likely if the patient stands (or sits up in bed) and for the same reason it is strongly recommended that the patient drink at least 100 ml of water with the medicine.
Patients sometimes have prejudices against particular colours. Some, for example, associate green with poisons; others feel that red tablets are particularly dangerous. Such fears can often be allayed by explanation.

The prescription of capsules to an elderly patient accustomed to tablets may cause misunderstanding; a patient may, for example, attempt to empty ampicillin out of its capsule before taking it. Moreover, some effervescent formulations may be swallowed dry instead of dissolved in water.

Size of dose

Age-related changes in the metabolism and excretion of a drug or its end organ responsiveness often mean that old people require much smaller doses. An example is nitrazepam, for which the dose recommended for elderly patients is 2.5–5 mg at night. They may be advised to take only half-tablets, but this is often easier said than done by a patient with failing eyesight and arthritic hands. There are advantages, therefore, in prescribing tablets that contain small doses. Examples include 62.5-mg capsules of levodopa with benserazide, 0.0625-mg tablets of digoxin and 12.5-mg tablets of hydrochlorothiazide.

Frequency of dose

Compliance is improved by prescribing a drug that can be taken once or twice rather than several times a day. Whether this is practicable for a given preparation will depend on its duration of action. One way of prolonging this is to dispense drugs in slow-release capsules. In young people this can often be relied on to prolong the duration of action to 12 hours. In old people the effect may be less predictable.

An alternative is to use a drug that is slowly excreted or metabolized. Reduced renal and hepatic function, however, can lead to cumulation and toxicity from some such drugs in old age. An example is the long-acting non-steroidal anti-inflammatory drug
piroxicam, which is more prone to cause gastric ulcers and haemorrhage in old people. Short-acting drugs such as ibuprofen, given several times per day, may be much safer.

There are many drugs for which a sustained clinical effect does not depend on maintaining a high blood concentration. This means that, although they may have a relatively short plasma half-life, single daily doses are all that may be required. Examples include tricyclic antidepressants given as a single evening dose, thioridazine or chlorpromazine given as a single evening dose, and corticosteroids given every second day. This approach is practicable only when relatively small doses are given. For example, if more than 75 mg of thioridazine is required, it should be given in divided doses.

Exceptions to the rule that doses several times a day should be avoided include drugs used in Parkinson’s disease; doses of levodopa may have to be given up to two-hourly to avoid the “on-off” pattern that often develops in more advanced disease.

Liquids

If patients have difficulty in swallowing tablets and capsules, then elixirs, mixtures, solutions, tinctures and syrups may be useful alternatives. There are also patients who derive greater psychological benefit from taking a brightly coloured bitter liquid rather than a white tasteless pill. Finally, drugs in liquid form can be mixed with food; for example an agitated, uncooperative and suspicious old person can be given haloperidol drops in tea or soup.

A limitation of liquids is that it is very much more difficult to give accurate doses. Patients may use the wrong size of spoon. Even if they use a standard plastic spoon they have to pour from a bottle, fill the spoon to the brim, and move the spoon up to their lips. This operation becomes difficult if the patient has poor vision, arthritis or a tremor. These problems can be partially resolved by issuing graduated plastic beakers.
Parenteral preparations

A major advantage of parenteral preparations over oral ones is that compliance is ensured. It is easier to maintain vitamin D levels with injections of 600 000 i.u. of ergocalciferol every 6 months than to persuade a patient to take 500 i.u. daily as tablets of calcium and vitamin D. Again, it may be easier to control agitation in an uncooperative patient with intramuscular injections of 25 mg of fluphenazine decanoate every 3 weeks than with a comparable neuroleptic given orally.

A disadvantage of long-acting parenteral injections is that, if there are side effects, they may take a long time to disappear. Hypercalcaemia from vitamin D intoxication persists for weeks, and oversedation from injected phenothiazine esters persists for days.

Intramuscular injections may also be extremely painful. Penicillin G, chlorpromazine and aminophylline are all extremely irritant. Intramuscular injections of iron are particularly unpleasant and should never be used if intravenous preparations are available; if compliance is poor and correction of iron deficiency important, the mineral should be given intravenously. Some drugs that act when given intravenously are ineffective by the intramuscular route.

If a patient is living at home, injections may have to be given by a relative or a community nurse. This is not always a disadvantage. Monthly injections of vitamin B₁₂ may, for example, give a community nurse a reason for looking in to see how a frail old person is coping alone.

In many countries, however, it is a common but misguided belief that drugs given parenterally are more effective than those given by any other route. This superstition should be challenged. Moreover, disposable syringes and needles are expensive and under unhygienic circumstances may contribute to the spread of HIV and hepatitis infection.
Other routes

Suppositories

Emaciated old people have little gluteal muscle left for intramuscular injections. Even where this is not the case, patients with nausea or acute pain may find repeated painful injections unacceptable. In such situations, drugs may be given per rectum. Preparations given by this route include antihaemorrhoidal preparations, ergometrine, indomethacin, mesalazine, metronidazole, chlorpromazine and paracetamol. Aminophylline suppositories still enjoy great popularity, but their use should be discouraged because theophylline absorption from this formulation is low and unpredictable.

When rapid action is required and the drug cannot be administered in any other way, it may be given rectally in liquid form, such as small enemas of corticosteroids in ulcerative colitis or diazepam in status epilepticus.

Inhalations

A wide range of drugs used in chronic airflow limitation are available as aerosol or microcrystalline powder inhalations. The patient must be carefully instructed in their proper use. Many old people have neither the mental function, the manual dexterity nor the respiratory coordination to cope with them. One approach to the problem is to attach the insufflator to an expanded airway. If the drug is insufflated into this it remains there for some time so that the timing of inspiration by the patient becomes less crucial. The diversity of design shows that the ideal solution has not yet been found, and further experience is required to see whether this approach is useful in old people.

Combination products

One way of simplifying medication and thus improving compliance is to combine different substances in one tablet.
Examples include beta-blocking agents combined with thiazide diuretics, thiazide diuretics combined with potassium-sparing agents, and tricyclic antidepressants combined with phenothiazine tranquillizers. These should only be used if one drug is inadequate. For example, moderate hypertension should be treated initially with either a thiazide diuretic or a beta-blocking agent and the other drug added only if the first is ineffective. Combination drugs, again, do not absolve the clinician from the responsibility of careful monitoring. Patients on thiazides and potassium-sparing agents may still become hypokalaemic or hyperkalaemic. A further problem is that, with combination products, it is impossible to tailor drug ratios to individual requirements. Economic considerations should not be allowed to override these principles.

**Alternatives to drugs**

Patients not keen to take vitamins or minerals as tablets or medicines can sometimes be persuaded to take them as supplements to their diet. For example, orange juice contains high concentrations of ascorbic acid, and orange juice or tomato juice high concentrations of potassium. Many fresh vegetables contain such ingredients, which may be destroyed by overcooking.

When patients adopt a healthier style of living, stop smoking and avoid drinking too much tea and coffee in the evening, many prescriptions for sleeping pills become superfluous.
Examples include beta-blocking agents combined with thiazide diuretics, thiazide diuretics combined with potassium-sparing agents, and tricyclic antidepressants combined with phenothiazine tranquillizers. These should only be used if one drug is inadequate. For example, moderate hypertension should be treated initially with either a thiazide diuretic or a beta-blocking agent and the other drug added only if the first is ineffective. Combination drugs, again, do not absolve the clinician from the responsibility of careful monitoring. Patients on thiazides and potassium-sparing agents may still become hypokalaemic or hyperkalaemic. A further problem is that, with combination products, it is impossible to tailor drug ratios to individual requirements. Economic considerations should not be allowed to override these principles.

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When patients adopt a healthier style of living, stop smoking and avoid drinking too much tea and coffee in the evening, many prescriptions for sleeping pills become superfluous.
An adverse drug reaction (ADR) is any harmful or unwanted effect caused by a drug taken as instructed in its regular dosage.

Old people are at particular risk of developing ADRs. To some extent this is due to the mere fact that old people in general take more drugs than the young. To this must be added the fact that elderly patients, owing to pharmacodynamic and pharmacokinetic changes as well as loss of reserve capacity and reduced homeostatic control, are more sensitive to the harmful effects of drugs. Poor compliance, being more common in old age, is another cause of side effects. So is multiple medication; one community study showed that the prevalence of side effects was 18% in those using fewer than 6 drugs and 80% in those using more than 6 drugs.

ADRs in elderly patients contribute to morbidity and not infrequently result in the patient’s deciding to withdraw from the treatment. Some 10–20% of patients admitted to geriatric departments suffer from side effects, and in 5–12% of such cases these were the main reason for admission. In this context, the most frequent causative drugs are diuretics, psychotropic drugs of all types, digitalis glycosides, non-steroidal anti-inflammatory agents (including aspirin) and antiparkinson drugs.

ADRs are frequently overlooked in the elderly. One main reason is that doctors tend to forget that virtually any symptom in an old person may be drug-induced or aggravated by drug treatment. The other is that, as a general rule, the diagnosis of ADRs is difficult, and perhaps especially so in the elderly.

The diagnosis of an ADR is based primarily on a meticulous drug history, the establishing of a temporal relationship between exposure to the drug and the clinical manifestations, and improvement on withdrawal or dosage reduction. Most
doctors have experienced the often insuperable problem of getting a precise drug history from an old person living alone. The best way of ensuring that reliable information is obtained is probably by making a home visit to see all the patient’s drugs. As a general rule patients should bring all their drugs with them whenever they enter hospital.

ADR s in the elderly often occur during the first 1–2 weeks after starting treatment or increasing the dose. There are, however, important exceptions to this generalization, such as disturbances of serum potassium due to diuretics, tardive dyskinesias after prolonged use of antipsychotic drugs, and acute leukae mia due to alkylating cytotoxics given many years earlier. Severe ADRs in the elderly are, in 9 out of 10 cases, due to a drug’s well known pharmacological effects, and are not infrequently precipitated by drug interaction. Allergic reactions, most commonly caused by antimicrobial drugs (e.g. ampicillin derivatives, sulfonamides) seldom give rise to therapeutic problems in the elderly. Allergic reactions can, however, produce difficult diagnostic problems if the patient presents with fever (drug fever) as the principal manifestation.

Abrupt withdrawal of certain drugs (benzodiazepines, beta-blockers) can cause severe reactions in the elderly.

Rechallenge is the most powerful diagnostic tool when a side effect is suspected. Severe and even fatal reactions can result from such experimentation, however, and rechallenge should for obvious ethical reasons be left to experts.

Geriatric practice is often complicated by the nonspecific symptomatology of disease in old age, the patient or the family characterizing the major symptoms as lassitude, weight loss, lightheadedness, urinary incontinence or confusion. All these symptoms can be drug-induced, and some frequent offenders are listed in Table 2.

Another complicating factor in geriatric medicine is that severe disorders so often start insidiously and are therefore easily overlooked by the patient as well as by relatives and the doctor. The most frequently overlooked disorders in the elderly
<table>
<thead>
<tr>
<th>Confusional states</th>
<th>Depression</th>
<th>Falls</th>
<th>Postural hypotension</th>
<th>Constipation</th>
<th>Urinary incontinence</th>
<th>Parkinsonism</th>
</tr>
</thead>
<tbody>
<tr>
<td>hypnotics</td>
<td>methyldopa</td>
<td>hypnotics</td>
<td>all antihypertensives</td>
<td>codeine</td>
<td>loop diuretics</td>
<td>antipsychotics</td>
</tr>
<tr>
<td>tranquilizers</td>
<td>reserpine</td>
<td>tranquilizers</td>
<td>diuretics</td>
<td>dextropropoxyphene</td>
<td>hypnotics</td>
<td>drugs for vertigo</td>
</tr>
<tr>
<td>antidepressants</td>
<td>beta-blockers</td>
<td>antidepressants</td>
<td>anti-anginal drugs</td>
<td>narcotics</td>
<td>tranquilizers</td>
<td>methylidopa</td>
</tr>
<tr>
<td>antipsychotics</td>
<td>tranquillizers</td>
<td>antipsychotics</td>
<td>beta-blockers</td>
<td>diuretics</td>
<td>antipsychotics</td>
<td>prazosin</td>
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<tr>
<td>anticholinergics</td>
<td>antihistamines</td>
<td>hypnotics</td>
<td>anticholinergics</td>
<td>anticholinergics</td>
<td>reserpine</td>
<td>metoclopramide</td>
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<tr>
<td>(centrally acting)</td>
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<td></td>
<td></td>
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<tr>
<td>non-steroidal</td>
<td>corticosteroids</td>
<td>carbamazepine</td>
<td>tranquilizers</td>
<td>disopyramide</td>
<td>labetalol</td>
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<tr>
<td>anti-inflammatory</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>drugs</td>
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<tr>
<td>levodopa</td>
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<tr>
<td>bromocriptine</td>
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<tr>
<td>antidiabetics</td>
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<tr>
<td>(hypoglycaemia)</td>
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<tr>
<td>corticosteroids</td>
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<tr>
<td>digitalis glycosides</td>
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<td></td>
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<tr>
<td>anticonvulsants</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>cimetidine</td>
<td></td>
<td></td>
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</tbody>
</table>

*Because of polyuria.
tend to be depression, cognitive defects (e.g. dementia) and parkinsonism, which can all be precipitated or aggravated by drugs (Table 2).

The best way of treating any patient with a suspected ADR is by drug withdrawal or dosage reduction under clinical surveillance. In some cases, where the patient deteriorates when the dose is reduced, it may be appropriate to prescribe an additional drug to control the side effects, such as potassium supplements for hypokalaemia caused by a diuretic, or anticholinergics for drug-induced parkinsonism. The widespread use of anticholinergic drugs to prevent neuroleptic-induced dyskinesias should be condoned, however, because further deterioration of symptoms is not uncommon. Minor complaints caused by side effects, such as dry mouth or slight palpitations during treatment with a tricyclic antidepressant, are usually no reason for withholding therapy and are normally easily handled by reassuring the patient. Quite often, the history and clinical examination of patients with side effects reveal that no valid indication for the offending drug has been present. A typical example is when an elderly patient develops parkinsonism that proves to be caused by the neuroleptic prochlorperazine given for dizziness, which turns out to be due to postural hypotension. In cases like this, diagnosing and treating an ADR by withdrawing a harmful and inappropriate drug are especially rewarding.

ADRs can to a large extent be avoided in the elderly by choosing safe and effective drugs and applying sound therapeutic principles in prescribing, such as starting with a small dose, observing the patient frequently and avoiding excessive polypharmacy.

Some drugs, such as barbiturates, should not be used at all in the elderly as they cause a lot of problems and are easily replaced by safer alternatives. Many drugs are hazardous for the long-term treatment of old people due to their low margin of safety (low therapeutic index) or because their elimination is either so slow that accumulation is most probable or is dependent on kidney function, which is so frequently reduced in the elderly. Examples of such drugs include the aminoglycoside antibiotics
for systemic use, amiodarone, chlorpropamide, digoxin, metformin, lithium, nitrofurantoin and perchexilene maleate. Table 3 lists some drugs with potentially severe or unusual side effects in old people.

Table 3. Drugs with potentially severe or unusual side effects in the elderly

<table>
<thead>
<tr>
<th>Drug</th>
<th>Unwanted effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>aminoglycoside antibiotics</td>
<td>deafness, renal failure</td>
</tr>
<tr>
<td>all barbiturates*</td>
<td>confusion</td>
</tr>
<tr>
<td>anticholinergic drugs (centrally acting)</td>
<td>visual and auditory hallucinations</td>
</tr>
<tr>
<td>e.g. trihexyphenidyl</td>
<td></td>
</tr>
<tr>
<td>cardiac glycosides</td>
<td>behaviour disorders, abdominal pain, fatigue, anorexia and weight loss, rhythm disorders</td>
</tr>
<tr>
<td>chlorpromazine</td>
<td>postural hypotension, hypothermia</td>
</tr>
<tr>
<td>co-trimoxazole</td>
<td>agranulocytosis, aplastic anaemia, serious skin reactions</td>
</tr>
<tr>
<td>disopyramide</td>
<td>urinary retention, constipation</td>
</tr>
<tr>
<td>enalapril (captopril) in cardiac failure</td>
<td>renal failure, first-dose hypotension</td>
</tr>
<tr>
<td>estrogens</td>
<td>fluid retention, congestive cardiac failure</td>
</tr>
<tr>
<td>flunarizine, cinnarizine</td>
<td>parkinsonism</td>
</tr>
<tr>
<td>furosemide</td>
<td>hypotension, cerebrovascular accidents</td>
</tr>
<tr>
<td>isoniazid</td>
<td>hepatotoxicity</td>
</tr>
<tr>
<td>lithium*</td>
<td>urinary incontinence, dehydration*</td>
</tr>
<tr>
<td>mefenamic acid</td>
<td>diarrhoea, liver damage</td>
</tr>
<tr>
<td>methyldopa</td>
<td>drowsiness and depression</td>
</tr>
<tr>
<td>nitrofurantoin*</td>
<td>peripheral neuropathy, lung reactions</td>
</tr>
<tr>
<td>non-steroidal anti-inflammatory drugs (some) e.g. azopropazine, ketoprofen, piroxicam*</td>
<td>gastrointestinal ulceration, haemorrhage and perforation</td>
</tr>
<tr>
<td>pentazocine*</td>
<td>confusion, variable efficacy</td>
</tr>
<tr>
<td>triazolam</td>
<td>confusion, psychotic reactions</td>
</tr>
</tbody>
</table>

* Drugs to be avoided in the elderly if possible.
* Because of polyuria.
Determinations of serum concentration, where available, have become a valuable tool in geriatric practice, where they serve as an adjunct both in the diagnosis of ADRs and undertreatment and in the routine surveillance of asymptomatic patients. Unfortunately, hypoproteinaemia and hypoalbuminaemia are common in sick old people, obscuring the interpretation of such data for highly protein-bound drugs. It may seem prudent, therefore, to aim initially at the lower half of the recommended therapeutic concentration range when titrating doses for the elderly according to serum concentrations. Drugs for which routine determinations of serum concentrations may be appropriate for the prophylaxis of side effects in the elderly are listed in Table 4.

Table 4. Drugs for which routine determinations of serum concentrations may be appropriate to avoid adverse drug reactions in the elderly

| Drug/
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>aminoglycoside antibiotics (systemic use)</td>
</tr>
<tr>
<td>anti-epileptic drugs</td>
</tr>
<tr>
<td>digitoxin</td>
</tr>
<tr>
<td>digoxin</td>
</tr>
<tr>
<td>disopyramide</td>
</tr>
<tr>
<td>lithium</td>
</tr>
<tr>
<td>theophylline</td>
</tr>
</tbody>
</table>

* Routine determination of serum concentrations must be performed in samples drawn at a standardized time after the last dose.

The establishment of the proper use and the safety of new drugs depends to a large extent on the spontaneous reporting by doctors of cases of suspected side effects. Life-threatening and unusual reactions believed to be caused by newly released drugs should always be reported to the national adverse drug reaction centre. Early recognition of some very typical disease entities as drug-induced may save lives. Life-threatening or unusual, possibly drug-induced disease entities include:
agranulocytosis
aplastic anaemia
anaphylactic shock
angioedema
Lyell’s syndrome (toxic epidermal necrolysis, exfoliative dermatitis)
Stevens-Johnson syndrome (erythema multiforme)
acute severe hepatitis
lactic acidosis (anion gap)
atypical ventricular tachycardia ("torsade de pointes") often preceded by prolongation of the corrected Q-T interval on the electrocardiogram (ECG).
Antacids and other drugs used for gastric disorders

Hiatus hernias are so common in old people that radiological evidence of one does not prove that this is the cause of symptoms.

Peptic ulcers may not present with pain in old people but give rise to nonspecific symptoms such as weight loss, anaemia or even confusion.

In some old people, peptic ulcer is drug-induced.

In old people there is an increased chance that a gastric ulcer will be malignant.

While old people usually take medication so long as they have dyspepsia, it is more difficult to ensure that they continue the treatment to heal an ulcer once symptoms subside.

Many drugs used to treat ulcers cause constipation.

Endoscopy and contrast radiography are uncomfortable, so that there is a temptation to treat old people symptomatically for long periods without an established diagnosis.

Inappropriate advice on diet may cause serious undernutrition.

Indications and prescribing rules

Non-specific dyspepsia

Occasional episodes of dyspepsia may be treated symptomatically with antacids. If symptoms persist a diagnosis should be confirmed by endoscopy or contrast radiography. Histamine $H_2$-receptor antagonists (e.g. cimetidine, ranitidine) are widely used, but should be prescribed only if a firm diagnosis has been made.

Hiatus hernia

Make sure that symptoms are due to the hiatus hernia itself and are not the result of gallstones or ischaemic heart disease. Supplement
drug treatment with advice on reducing weight, sleeping with the bed propped up and eating in an upright chair.

Antacids are useful, particularly if there is clinical or endoscopic evidence of peptic oesophagitis. If symptoms do not subside, a histamine H₂-receptor antagonist or omeprazole should be used.

**Benign stricture of the oesophagus**

There is no evidence that histamine H₂-receptor antagonists are of any value in this complication of hiatus hernia.

**Gastric ulcer**

Make sure that the ulcer is benign before embarking on an anti-ulcer regime. Histamine H₂-receptor antagonists heal about two thirds of gastric ulcers but they tend to have to be continued indefinitely. If there is evidence for *Helicobacter pylori* infection, this may be treated with a combination of antibiotics, acid production inhibitors and bismuth subcitrate, but results in the elderly are not entirely satisfactory and the side effects of this combination treatment should be taken into account.

**Duodenal ulcer**

Antacids relieve the symptoms of a duodenal ulcer. If taken in massive doses, they can be used to heal it, but most old people often fail to comply with such a regime. Histamine H₂-receptor antagonists and omeprazole are now the preparations of choice.

**Classes of drug**

**Antacids**

Magnesium oxide and hydroxide mixtures are effective antacids. In old people they have the additional advantage of having a mild laxative effect. For the control of symptoms the dose is
15–30 ml, half an hour before meals and at bedtime. For healing an ulcer the dose is 30 ml, 1 and 3 hours after meals and at bedtime.

Aluminium hydroxide mixture, given in the same doses, is also effective but gives old people constipation. The prolonged use of high doses must be avoided, since the effects on phosphate metabolism may promote decalcification of bone.

A host of other antacids is available, but these are no more effective than the two already mentioned.

**Histamine H₂-receptor antagonists**

Cimetidine is given in a dose of 200 mg (0.2 g) 3 times daily and 400 mg (0.4 g) at bedtime for 6 weeks, followed by a maintenance dose of 400 mg (0.4 g) at bedtime. The oral form occasionally causes confusion, but most old people tolerate it well. Interactions with other drugs such as anticoagulants and beta-blockers may present further problems. Intravenous cimetidine is not of proven value in stopping bleeding, and can cause confusion in the elderly.

Ranitidine is more expensive than cimetidine, and it is given in a dose of 150–450 mg (0.15–0.45 g) twice daily. It is theoretically less likely to cause confusion or interact with other drugs. Practical experience has not shown substantial benefit of ranitidine over cimetidine or other histamine H₂-receptor antagonists such as famotidine, nizatidine or roxatidine. The latter have no advantage over the standard drugs and experience with them is far more limited.

**Other types of drug**

Omeprazole is a so-called proton pump inhibitor and a more effective inhibitor of gastric acid production than the histamine H₂-receptor antagonists. It has proven to be particularly effective for the treatment of reflux oesophagitis, but has no advantages over histamine H₂-receptor antagonists for the symptomatic treatment of duodenal and gastric ulcer.
Bismuth subcitrate is useful both in functional dyspepsia and in peptic ulcer but, except as part of the combination treatment of *Helicobacter pylori* infection, has been largely superseded by other drugs. Bismuth is a toxic substance and some is absorbed; the drug is therefore not suitable for maintenance treatment.

Anticholinergic drugs are of value only in occasional cases.

**Alternative treatment**

The diet should be examined and corrected as necessary, but milk diets are not of proven value and may worsen the condition. Smoking should be stopped and the use of alcohol and coffee moderated.
Anti-emetic drugs

Vomiting may be the result of intestinal obstruction, uraemia, pyloric stenosis, drug intoxication or faecal impaction. The vomiting associated with cancer chemotherapy can cause great distress, as can vomiting of unknown origin.

Nausea responds to the same forms of treatment as vomiting.

Oral therapy is clearly of little value if vomiting leads to loss of the ingested dose.

Classes of drug

Chlorpromazine is effective (starting dose 25–100 mg, rising if necessary to 300 mg) but can cause occasional jaundice. Metoclopramide is another useful drug (5 mg up to 3 times per day), as is prochlorperazine. Injections are painful. Remember that all these drugs are neuroleptic-related and can cause extrapyramidal symptoms.

A new group of drugs has been introduced to prevent and treat nausea and vomiting associated with cancer chemotherapy, particularly cisplatin-containing regimes. Its prototype is ondansetron. They are less useful in preventing late (“delayed”) vomiting but have been successfully combined with older standard anti-emetics such as prochlorperazine, lorazepam and dexamethasone.
Drugs in the treatment of bowel disorders

Constipation

Constipation is not a problem in fit old people. Some, however, become obsessed with bowel function and take regular doses of powerful laxatives. The colon eventually becomes insensitive to laxatives and severe constipation ensues. In severe cases colonic nerve plexuses may be destroyed.

Patients with limited mobility, with pelvic muscle wasting and with a low intake of fluids and solids are at particular risk from constipation.

In severe constipation, faeces in the rectum and colon become hard, dry and impacted. Complications of faecal impaction include subacute obstruction, severe discomfort and spurious diarrhoea associated with faecal incontinence.

As many drugs may cause or worsen constipation (iron salts, anticholinergics or drugs with anticholinergic side effects, opiates), such possible causative agents should be eliminated before treatment is started.

Indications and prescribing rules

Frail old people at risk of developing constipation should be treated with bulking agents.

If the rectum is loaded and bulking agents are ineffective, the patient should be given a short course of treatment with a stimulant laxative or suppository.

If the faeces are hard and dry, a stool-softening agent should be added to the regime.

If there is severe impaction, an enema should be used. A soap and water enema, however, should never be used: it may cause severe fluid and electrolyte imbalance and kill the patient.
Laxatives are clearly needed in myocardial infarction and haemorrhoids in order to avoid straining.

**Classes of preparation**

**Bulking agents**

Bran can be purchased as a cheap and readily available commodity and taken in a dose of 10 g twice daily with meals. The starting dose should be lower to avoid colic. Psyllium seeds are an alternative to bran. Several proprietary preparations of bulking agents are available.

**Osmotic agents**

Lactulose is a sugar that draws fluid into the colon by osmosis. Bacterial interaction produces gas, so that old people are often distressed by borborygmi, colic, flatulence and abdominal distension. The dose is 15 ml twice daily, reduced according to requirements.

**Stimulant laxatives**

All of these sometimes cause cramps.

<table>
<thead>
<tr>
<th>Form</th>
<th>Daily dose at bedtime</th>
</tr>
</thead>
<tbody>
<tr>
<td>senna</td>
<td>tablets, granules or syrup</td>
</tr>
<tr>
<td>bisacodyl</td>
<td>coated tablets</td>
</tr>
<tr>
<td>sodium picosulfate</td>
<td>elixir or enema</td>
</tr>
</tbody>
</table>

Phenolphthalein and phenolphthalein-containing combination laxatives should no longer be used.

**Faecal softeners**

Docusate sodium is a detergent that mixes with and softens faeces. It is taken as tablets or a syrup in a dose of 12.5–50 mg
3 times daily, but a single higher dose (200 mg) given once a day is also acceptable.

The use of liquid paraffin should be abandoned altogether. Complications include faecal leakage, aspiration pneumonitis and a fat-soluble vitamin deficiency.

**Suppositories and enemas**

Suppositories useful in faecal impaction include bisacodyl. There are also various phosphate enemas or microenemas available, as well as docusate sodium.

**Alternatives to drugs**

Healthy old people should be encouraged to regulate bowel function without recourse to drugs. Measures include taking physical exercise; obeying calls to stool; passing motions at a regular time, preferably after meals; and taking a high-fibre diet along with plenty of liquid.

**Diarrhoea**

Diarrhoea may be a symptom of underlying infection (see page 91) or have specific organic causes (requiring investigation); it may also be an adverse reaction to various drugs or result from laxative abuse. One particular danger is the diarrhoea resulting from chronic, often secretive use of laxatives obtained without prescription, some of which are sold as slimming remedies. Diarrhoea attacks in nursing homes should be carefully investigated and possible common sources of infection identified and properly treated.

Mild transient diarrhoea should not be treated with drugs. Replacement of fluid loss, whether by using dissolved oral rehydration salts or equivalent volumes of tea, broth, thin soup or lemonade, is all important in the elderly.
Classes of preparation

Centrally acting agents

When needed, an opium alkaloid (tincture of opium or codeine phosphate) is suitable. Loperamide has similar effects but is regarded as much less likely to cause sedation and addiction. If it is likely that the diarrhoea is of bacterial origin (i.e. Salmonella, Campylobacter) a three-day course of a suitable antibiotic (co-trimoxazole, norfloxacin or ciprofloxacin) should be added and fluid intake should be ample.
Drug treatment of incontinence and other disorders of micturition

The pharmacological management of functional bladder incontinence is still far from satisfactory. So far anticholinergic drugs are the only ones that have been found to be useful, but it has proved almost impossible to separate systemic anticholinergic effects (dry mouth, blurred vision, obstipation, tachycardia and mental disturbances) from the local effects on the bladder. Emepronium bromide and terodilone have been withdrawn for safety reasons. Oxybutynin is effective in some patients with incontinence due to detrusor instability, and a small dose (5 mg twice daily) is worth a try if other measures have been ineffective. Side effects are still common, however, and patient compliance is therefore often poor.

Benign prostatic hypertrophy is extremely common in men from the age of 50 onwards but drug treatment can often be postponed for many years. The alpha₁-blockers prazosin, doxazosin and terazosin reduce symptoms by decreasing internal sphincter tone and inhibiting smooth muscle contraction but their systemic effects make these drugs less practicable for long-term treatment. A related drug, alfuzosin, is claimed to act predominantly locally and to produce less dizziness and hypotension. Although subjective improvement is often quite good, the improvement in urinary flow rate remains modest.

Anti-androgens, particularly drugs that block the peripheral conversion of testosterone to dihydrotestosterone, are now also being used. Except for impotence and loss of libido in about 5% of patients, side effects are minimal. Again, the effect is modest and unpredictable, but the drug can be used in patients who refuse or cannot undergo an operation.
Antidiabetic drugs

The objectives of treating diabetes in the elderly are the same as in the young, i.e. the relief of symptoms, the prevention of the complications of the disease and its control during emergencies.

Two types of elderly diabetic patient are encountered: the first is the diabetic (often insulin-requiring) who has grown old with the disease, and the second the patient with newly discovered disease, who may be thin or fat. Diabetes may rarely result from long-term therapy with diuretics of the thiazide type or with steroids, and may not remit when they are discontinued.

Most people develop an impairment of glucose tolerance as they grow older, but only a few have true diabetes mellitus requiring treatment. Care should be taken to distinguish between these two groups, since only a small proportion of people with impaired glucose tolerance develop diabetes, and many spontaneously revert to normal; they have a much greater islet-cell reserve than diabetics.

The physiology of the disease is essentially the same as in younger people, except that there may be a high renal threshold for glycosuria; this means that urine testing may be less reliable as a control measure than in younger people. The complications of the disease are the same as in the young, but are if anything more frequent. They include retinopathy, neuropathy (including amyotrophy), nephropathy, arterial disease and cataracts.

Indications and prescribing rules

The indication for drug treatment of diabetes is significant hyperglycaemia and glycosuria persisting despite adequate dietary treatment.

Most elderly patients who have grown old with their disease require insulin, but relatively few of those who develop the disease late in life will need it. Some of the latter will require oral therapy; insulin will be necessary during diabetic emergencies.
The therapeutic approach to diabetes developing late in life is easier where the condition is a complication of obesity and can be treated by proper attention to diet. This will render oral therapy unnecessary in many cases.

**Classes of drug**

**Sulfonylureas**

The most used include tolbutamide, glibenclamide and glipizide, which have a relatively short action (see Table 5) but can nevertheless be given as a single dose before breakfast.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shorter-acting (2–4 doses daily)</td>
<td></td>
</tr>
<tr>
<td>glibenclamide</td>
<td>5–45</td>
</tr>
<tr>
<td>glipizide</td>
<td>2.5–7.5</td>
</tr>
<tr>
<td>gliquidone</td>
<td>15–45</td>
</tr>
<tr>
<td>glymidine sodium</td>
<td>500</td>
</tr>
<tr>
<td>tolazamide</td>
<td>100–500</td>
</tr>
<tr>
<td>tolbutamide</td>
<td>500–1500</td>
</tr>
<tr>
<td>Longer-acting (1 dose daily)</td>
<td>(to be avoided in the elderly)</td>
</tr>
<tr>
<td>chlorpropamide</td>
<td>12.5–75</td>
</tr>
<tr>
<td>glibornuride</td>
<td></td>
</tr>
</tbody>
</table>

Where still available, chlorpropamide, which is excreted by the kidney and may therefore cumulate seriously, especially in renal failure, should not be used; it may cause severe and prolonged hypoglycaemia (with the possibility of irreversible cerebral damage), hyponatraemia, water retention and alcohol intolerance.

Start treatment with a short-acting compound before trying to control the patient on a long-acting compound.
The most common side effects to these drugs are drug rashes and hypoglycaemia. Major interactions are those with anticoagulants (bleeding) and sulfonamides (hypoglycaemia).

In all cases there is a maximum effective dose, but this may be up to ten times the minimum effective dose; the lowest possible effective dose should therefore be prescribed.

In many patients the response to sulfonylureas declines with age.

**Biguanides**

These are now restricted to metformin; since despite repeated warnings lactic acidosis can occur in the elderly and the drugs are contraindicated in cardiac, renal and hepatic disease, biguanides are best avoided altogether.

The side effects of the biguanides include anorexia and diarrhoea. The former was claimed to be of some use in weight reduction in diabetics.

**Insulin**

Many forms are now available, but the trend is towards fewer forms and one single strength (100 units per ml) rather than the various strengths previously used for many years. This development has been accelerated by the almost universal introduction of the insulin pump.

The varieties may be divided into short-acting, intermediate, long-acting and combinations (see Table 6). Soluble insulin should always be used in diabetic emergencies requiring insulin, while in maintenance therapy in those few elderly patients who require insulin it is best to employ long-acting or combination therapy. One rather than two or more injections per day should be preferred in elderly patients.

The long-term management of insulin-requiring diabetes in old age may be a matter of some difficulty. The dose needs to be adjusted to the patient’s changing nutritional requirements. The
avoidance of hypoglycaemia is more important than that of hyperglycaemia, although there is no doubt that good control of the latter helps prevent the long-term complications of the disease in the elderly, as well as in younger patients.

Some patients maintained on insulin earlier in life will later have to be switched to the more purified insulins for better control or to overcome insulin resistance. Biotechnologically manufactured human insulin has been used successfully in new cases and, despite its higher cost, its use will probably increase. Nevertheless, there is no stringent need for such a change in patients who have been well regulated on purified porcine insulin for many years.

<table>
<thead>
<tr>
<th>Variety</th>
<th>Peak action (hours)</th>
<th>Duration of action (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting soluble</td>
<td>2–4</td>
<td>6–12</td>
</tr>
<tr>
<td>Intermediate isophane insulin</td>
<td>5–12</td>
<td>12–25</td>
</tr>
<tr>
<td>Intermediate insulin zinc</td>
<td>3–6</td>
<td>12–16</td>
</tr>
<tr>
<td>Intermediate suspension (amorphous)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-acting protamine zinc</td>
<td>5–14</td>
<td>24–30</td>
</tr>
<tr>
<td>Combinations short + intermediate insulin zinc suspension</td>
<td>2–10</td>
<td>18–20</td>
</tr>
<tr>
<td></td>
<td>3–8</td>
<td>16–24</td>
</tr>
</tbody>
</table>
Vitamins

Many old people in different cultures are at a high risk of vitamin deficiency: those over 75, those who live alone, the confused, those who have recently been discharged from hospital, and those who are immobile and therefore cannot shop for their own food, as well as some in long-term institutional care.

Each of these factors is important; the more adverse factors that exist, the greater the risk. Multiple vitamin lack is usual; an isolated lack of one food factor is rare in the absence of obsessional food habits.

There is a good case for the prophylactic use of vitamin supplements in those at risk, especially during the winter months. Any reasonably priced multivitamin preparation that contains no more than 1000 i.u. of vitamin D and is without folic acid is suitable.

There is no evidence that vitamin therapy is of value in the treatment of confusion (except where this results from a specific clinically identifiable lack) or in the treatment of malignant disease or disease of the coronary arteries. The use of large doses of thiamine is, however, of undoubted value in the prevention and treatment of acute Wernicke’s encephalopathy.

Vitamin B group

Vitamin B<sub>12</sub> is dealt with under Drugs for anaemia (page 62).

Deficiency of other B vitamins is difficult to diagnose. Florid pellagra and beriberi are rare but the former is not. The aging skin is often dry; excessive dryness, cracking or scaling is suspicious. Riboflavin deficiency is common and should be thought of if milk intake is poor. A good multivitamin preparation as defined above is the treatment of choice where any vitamin B deficiency is found.
Vitamin C

Scurvy is still common, mainly in those who cannot, do not or choose not to eat fruit and in those who do not eat potatoes or who overcook them. It may be difficult to diagnose in the elderly since edentulous gums do not become spongy or bleed, and sheet haemorrhages may be absent. Delayed healing occurs.

Any role of high-dose vitamin C is open to informed doubt. It does not prevent the common cold or cancer.

Vitamin D and analogues

Osteomalacia is not uncommon in the Northern hemisphere; it is dealt with on page 51.

Vitamin E

Limited-scale intervention studies do not support the notion that vitamin E deficiency causes clinical symptoms except in some people with malabsorption syndromes. Ongoing studies in cancer patients have not so far produced any positive results. There is no case for dosages exceeding the recommended dietary allowance of about 10 mg per day.
Drugs for osteoporosis and osteomalacia

It is extremely difficult to monitor the effects of drugs on the bone. Radiological and absorptiometric techniques are insufficiently sensitive to identify changes in bone thickness in individual patients. Serial bone biopsies are unjustified. Treatment often has to be continued without any clear short-term indication of benefit. There is no evidence that any treatment, prophylactic or otherwise, is indicated in adult males.

Parenteral calcium should not be used in the old; it can cause hypercalcaemia.

Indications and prescribing rules

Pre-existent osteomalacia and osteoporosis need treatment, if only in an attempt to prevent them getting worse. The value of preventive postmenopausal treatment in women who have had little physical exercise and have used a low-calcium diet for many years before the menopause is now firmly established.

At present the only treatment that can be recommended for routine use in osteoporosis is estrogen supplementation.

Calcium

Calcium reduces bone loss in some postmenopausal women when given together with hormone replacement therapy, but there are no guidelines as to which postmenopausal women may benefit. No benefit accrues from calcium supplementation as a single treatment.

When giving calcium, review other drugs (such as tetracyclines and cardiac glycosides) being given to the patient, as calcium may interact with them.

Make sure that a calcium supplement is palatable, so as to avoid compliance problems. Most patients prefer effervescent calcium.
<table>
<thead>
<tr>
<th>Calcium per tablet</th>
<th>Daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>calcium gluconate</td>
<td>600 mg</td>
</tr>
<tr>
<td>calcium gluconate effervescent</td>
<td>400 mg</td>
</tr>
</tbody>
</table>

**Estrogens**

Estrogens normally inhibit bone breakdown by restraining the dissolution of collagen. It has been shown that, in premenopausal women who have undergone oophorectomy, bone loss can be prevented by small doses of estrogen; by analogy there is irrefutable evidence that estrogens given after the natural menopause prevent the development of osteoporosis.

Where severe and symptomatic osteoporosis is already present, estrogens can be given, e.g. conjugated estrogens 625 µg (0.625 mg) daily or ethinylestradiol 25 µg (0.025 mg) daily, both given cyclically and preferably balanced by progestogen.

Alternatively, estrogens can be administered in skin patches for transdermal delivery, avoiding first-pass metabolism of the hormones. Estrogens should be combined with oral calcium supplementation.

**Alternatives to calcium**

**Vitamin D**

Vitamin D increases calcium absorption, and it should probably be added when osteoporosis is treated with calcium supplements. In osteomalacia the simplest regime is to give 15 mg of ergocalciferol parenterally, repeating this after 6 months if necessary.

**Calcitriol and alfalcacicaldol**

These ergocalciferol metabolites also increase calcium absorption. Their role in osteoporosis is not yet clear. Patients on these agents have to be carefully monitored for hypercalcaemia.
**Thiazide diuretics**

Thiazide diuretics (e.g. hydrochlorothiazide, bendroflumethiazide) enhance the reabsorption of calcium ions from the urine, and some studies show that this confers beneficial effects in both female and male patients on long-term antihypertensive treatment with such drugs. The side effects do not warrant the use of thiazides in patients who do not need diuretic treatment.

**Sodium fluoride**

Sodium fluoride, given along with calcium and vitamin D, has been advocated in the management of osteoporosis. This regime should be avoided, because the quality of the bone tissue so formed is deficient.

**Anabolic steroids**

There is limited evidence that anabolic steroids not only prevent bone loss but may actually increase bone density. Androgenic side effects are unacceptable to many women, however, and the long-term effect is still unknown. Moreover, prolonged use of 17-β-substituted androgens carries a risk of hepatic damage (peliosis, hepatitis and liver cancer) and they cannot therefore be recommended.
Potassium

The object of potassium replacement is to replace a true potassium deficit (which may be defined as a deficient cell content of the ion), not reduced total body potassium (due solely to a reduction in cell mass).

The causes of potassium deficiency in the elderly are excess urinary losses due to diuretics or diabetes, and excess gastrointestinal loss due to diarrhoea. The frequently lower dietary potassium intake of the elderly is occasionally the sole cause; more often it is a contributory cause, because of failure to replace these excess losses.

Refractory potassium deficiency is occasionally related to magnesium depletion.

Indications and prescribing rules

Potassium replacement should be undertaken if there is low serum or red cell potassium in the presence of a cause of depletion.

Potassium depletion is often associated with a hypochloraemic alkalosis, and it is therefore important that replacement should be with potassium chloride.

Remember to treat the patient and not the serum potassium. Potassium replacement should be by the oral route unless the patient cannot take fluids or speed is considered essential, when potassium should be given by slow intravenous infusion.

Serum potassium levels should be monitored in all patients receiving potassium supplements. These should never be combined with potassium-sparing diuretics or spironolactone; the resulting hyperkalaemia has caused some deaths.

Classes of drug

The preparations widely used are slow-release potassium chloride and effervescent potassium chloride. The potassium
content of these is 6–12 mmol per tablet; at least 4–6 tablets per day are necessary. Tablets and capsules should be swallowed with ample fluid because they might otherwise cause oesophageal and gastric erosions and ulcers.

Intravenous potassium is given as potassium chloride solution: 20 mmol in 500 ml of 5% dextrose or half normal saline solution can be given over 4–6 hours.

Alternatives to potassium

Formal oral potassium therapy can be replaced by the administration of good natural sources of the ion, such as orange juice or concentrated tomato juice.

Where diuretics cause clinically relevant hypokalaemia (≤ 3.0 mmol/l), potassium-sparing diuretics can be added. The routine use of combination preparations of thiazide diuretics and such potassium-sparing drugs is generally not warranted.
Sodium

Sodium retention occurs, together with fluid retention, in cardiac failure, in renal disease, when drugs that contain a large quantity of sodium (such as sodium salts of salicylates and penicillins) are given, or following the use of some of the non-steroidal anti-inflammatory drugs and antihypertensive agents.

Treatment is with a diuretic and the withdrawal of any causal drug. Sodium retention is not synonymous with hypernatraemia; this may occur when either water intake has been too low or when there is a deficiency of antidiuretic hormone.

Sodium depletion (which is not synonymous with hyponatraemia) occurs as a result of severe diarrhoea, in adrenal (or anterior pituitary) failure, and following inappropriate exertion or exposure to severe heat.

Treatment is with intravenous sodium if the need is truly urgent, and otherwise with oral rehydration salts, sodium chloride tablets (300 mg (0.3 g) 3 times daily) or with a high dietary intake of salt.
Anabolic steroids

The anabolic steroids were developed from the male hormone testosterone, and are claimed to retain the latter’s effects on protein anabolism while having a less masculinizing effect.

In the doses normally recommended they simply act as weak androgens. They appear to have some “psychotonic” effect, encouraging the convalescent or ailing patient to eat and become more active. In elderly women, disturbing masculinizing side effects such as growth of facial hair or deepening of the voice may occur.

There is no proof of the long-term value of these drugs in most of the conditions, such as a lack of sexual potency, for which they have acquired a reputation, but they increase bone density in osteoporosis (see page 51). The clinical relevance of this effect is uncertain. In view of the hepatotoxicity of 17-β-substituted androgens, such drugs should be avoided.
Anticoagulant and antithrombotic drugs

Despite widespread application, the use of anticoagulants (heparin and the coumarin anticoagulants such as warfarin) and in particular the antithrombotic drugs has not been much studied in old age, where venous and arterial thromboembolisms are common.

Adverse reactions, notably haemorrhages, are more common in old people owing to increased sensitivity to vitamin K antagonists (dietary insufficiency of vitamin K or hepatic dysfunction) as well as to heparin (pharmacokinetic changes in the aged). Side effects are often precipitated by interaction, typically when an anticoagulant has been given with aspirin or some of the non-steroidal anti-inflammatory agents.

Poor compliance or the failure of the patient to appear for laboratory control often makes chronic treatment with anticoagulants impracticable in old people, however clearly indicated it may be.

Streptokinase and some of the newer biotechnologically manufactured thrombolytic agents entail a high risk of bleeding in old people and should be used only for the early treatment of acute myocardial infarction.

Platelet aggregation inhibiting agents such as low-dose (30–80 mg/day) aspirin are of great value in the prevention of stroke, particularly transient ischaemic attack in elderly patients, although even such small amounts may cause gastrointestinal haemorrhage in some patients. This is particularly the case in those with a history of ulcer disease. Adding dipyridamole to prophylaxis adds to the cost but not to the effect.

Indications and prescribing rules

Acute pulmonary embolism or deep vein thrombosis are the clearest indications for anticoagulants in old age.
Short-term prophylaxis with subcutaneous heparin, intravenous dextran or coumarin anticoagulants (which, however, should not serve as an alternative to early mobilization) is believed to reduce postoperative venous thromboembolism after major elective surgery, e.g. of the abdomen or hip joint, in old age. Both coumarin anticoagulants and heparin are safe and effective in preventing thromboembolism in hospital patients with acute myocardial infarction, but here, too, early mobilization is desirable.

Long-term prophylaxis is feasible only in a proportion of cases, where anticoagulants are not contraindicated. It may be considered for atrial fibrillation (with coumarin anticoagulants), particularly after strokes thought to be embolic; for patients with artificial cardiac valve prostheses (with coumarin anticoagulants); and possibly after transient cerebral ischaemic attacks (with coumarin anticoagulants or acetylsalicylic acid). Although some evidence exists favouring long-term prophylaxis with coumarin anticoagulants, acetylsalicylic acid or sulfinpyrazone after myocardial infarction, this cannot be recommended for the very elderly.

Anticoagulants and antithrombotic drugs are of no proven value in dementia, angina pectoris or intermittent claudication.

Reduction of dosage is usually necessary in old people. The oral anticoagulants such as warfarin act indirectly by vitamin K antagonism, and 3–4 days are therefore needed for the full effect to develop. In acute pulmonary embolism or deep vein thrombosis, initial treatment is usually given with heparin, since this acts immediately; the oral anticoagulant is then added and heparin withdrawn once the warfarin effect is established.

Heparin has to be given subcutaneously or intravenously. It must never be administered intramuscularly owing to the high risk of muscular haemorrhage.

The prescriber should be wary of interaction. Heparin, as well as the coumarin anticoagulants, should be given in reduced dosage if the patient is on acetylsalicylic acid or any other inhibitor of platelet function (non-steroidal anti-inflammatory
agents, dipyridamole). The coumarin dosage should be decreased if the patient is receiving certain antiarrhythmic drugs (e.g. amiodarone, quinidine).

**Classes of drug**

**Heparin**

*Usual dose in the elderly*

<table>
<thead>
<tr>
<th>Type</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>therapeutic</td>
<td>15 000–25 000 i.u. every 24 hours intravenously, or 7500–10 000 i.u. 3 times daily (12 000 i.u. twice daily) subcutaneously</td>
</tr>
<tr>
<td>prophylactic</td>
<td>5000 i.u. 2 or 3 times daily subcutaneously</td>
</tr>
</tbody>
</table>

Therapeutic anticoagulation with heparin is monitored using activated cephalin clotting time or thrombin clotting time, aiming at the same degree of anticoagulation as in younger patients.

Prophylaxis can be provided without laboratory control. Haemorrhages are usually controlled by withdrawing treatment and giving blood transfusions if necessary.

**Coumarin anticoagulants**

*Usual dose in the elderly*

<table>
<thead>
<tr>
<th>Type</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>initial doses</td>
<td>5–10 mg on day 1, slightly less on day 2</td>
</tr>
<tr>
<td>maintenance dose</td>
<td>up to 10 mg daily according to laboratory control</td>
</tr>
</tbody>
</table>

Dosage is adjusted according to the prothrombin clotting time, aiming at the same degree of anticoagulation as in younger patients:

- Thrombotest activity, 5–10%
- rabbit brain thromboplastin time, 2.0–4.5 times control value.
Mild haemorrhages are managed by withdrawal alone. More severe cases are given vitamin K (phytomenadione) 1–5 mg intravenously, which is effective after about 6 hours. Severe haemorrhage is managed by blood transfusion, which has an immediate effect by supplying normal clotting factors.

Surgery and dental extractions should not be performed at Thrombotest values below 12%.

**Platelet function inhibitors**

*Usual dose in the elderly*

- acetylsalicylic acid 30–100 mg once daily (prophylactic)

The optimum dosage for prophylaxis in transient ischaemic attacks is in the lower range.

No laboratory control is necessary. Nevertheless, gastrointestinal haemorrhages can be precipitated, so this prophylaxis is not suitable for a patient with a peptic ulcer or symptomatic hiatus hernia.

**Dextran**

Dextran have some use in the prophylaxis of thromboembolism after major orthopaedic surgery. Owing to the risks of fluid overload and anaphylactic reactions, however, heparin is probably a safer approach in the elderly. Dextran should not be given in impaired renal function.

No laboratory control is necessary when dextran are used.

**Alternatives to drugs**

For the prophylaxis of thrombotic complications, early mobilization is recommended. In deep vein thrombosis the swollen leg should be elevated until oedema is controlled; graduated compression stockings are then fitted and the patient mobilized.
Drugs for anaemia

The cardinal rule in the treatment of anaemia in the elderly is that the diagnosis should be complete and correct. Only anaemias with a haemoglobin concentration of less than 12 g/100 ml (11.5 g/100 ml in women over 75 years of age) should be treated. Many anaemias in the elderly are secondary, e.g. to hypothyroidism or scurvy, and although rarely severe they will not respond until their cause is found and treated. There is no indication for the use of vitamin B₁₂ as a “tonic” or as a treatment for senility, and it is of no value in post-herpetic neuralgia or peripheral neuropathies (unless the latter are due to subacute combined degeneration of the cord). Vitamin B₁₂ has in fact only one major indication, i.e. megaloblastic anaemia; it is also useful in tobacco amblyopia.

Indications and prescribing rules

Not all oral iron preparations are well tolerated, but it is virtually always possible to find a preparation that is. Iron can be given intravenously as a total dose infusion, based on the magnitude of the estimated deficit. This is suitable for outpatient and day hospital management, as well as in hospital, and reduces to zero the need for drug compliance in the early stages.

Folic acid should never be prescribed alone, except in pregnant women and in the unlikely event that regular checks on vitamin B₁₂ levels are feasible. Combined iron and folate tablets should not be given.

Classes of drug

Iron

There are many preparations of oral iron (generally based on ferrous sulfate, fumarate or gluconate). A dose of 100 mg per day of elemental iron continued for 3 months is adequate to
replenish iron stores in the presence of the severest deficiency, and it does not greatly matter which salt is used, provided the preparation is well absorbed and reasonably well tolerated. Some of the cheapest, least sophisticated preparations are the best.

Iron for intravenous use is generally given as iron sorbitol complex diluted in saline, over several hours; oral iron should be discontinued beforehand. Intramuscular injections should be avoided, as they cause discolouring of the skin and possibly local carcinogenicity.

**Folic acid**

This should be given initially in a dose of 5 mg per day, and as 0.1 mg per day for maintenance purposes. There is no advantage in larger doses.

**Vitamin B₁₂**

For pernicious anaemia this should be given intramuscularly in doses of 250 mg (0.25 g) as hydroxocobalamin. Doses should initially be given twice weekly for 2 weeks and thereafter every 3 months; this has the advantage that the district nurse’s visit to give the injection can be used for supervision if needed. There is no advantage in larger doses; very small doses may be used for diagnostic purposes.
Cardiac glycosides

Problems arise from an age- and disease-related increase in the serum half-life of digoxin, owing to delayed renal excretion and possibly also to a reduction in hepatobiliary excretion. There are important interactions with potassium and magnesium depletion, both due to diuretics, which potentiate the cardiac toxicity of the drugs. There is probably an increased frequency of central nervous system toxicity (confusion, nausea, vomiting, dizziness and occasionally xanthopsia) and of life-threatening cardiovascular complications, particularly arrhythmias, partly because of the high frequency of organic heart disease in the elderly.

Where a cardiac glycoside appears ineffective, the serum concentration should be checked to detect possible non-compliance or under-dosage.

Indications and prescribing rules

Cardiac glycosides are indicated for the control of a rapid ventricular rate in atrial fibrillation, with or without cardiac failure, and for cardiac failure in sinus rhythm, at least for some 6–12 weeks. There is doubt about the long-term usefulness of cardiac glycosides in cardiac failure. There is no truth in the belief, still strong in some countries, that the healthy aged heart requires digitalis as a tonic.

Cardiac glycosides are often given in an initial loading dose, determined mainly by the size of the patient and the need for fast action, and continued in a maintenance dose whose magnitude, in the case of digoxin, depends on the patient's current renal function. This may be assessed from serum creatinine levels. If this is less than 140 μmol/l (1.58 mg/100 ml), doses of 250 μg (0.25 mg) per day of digoxin are correct; if levels are higher than these, 125 μg is the correct daily dose.

Digoxin should only be administered intravenously in serious emergencies where an immediate effect is both essential...
and possible, such as in rapid atrial fibrillation or flutter with resulting cardiac failure.

Therapeutic ranges for serum concentrations are 1.0–2.5 µg/l (1–2 nmol/l) for digoxin and 12–25 µg/l (15–35 nmol/l) for digitoxin. Levels below the lower limits are rarely effective; levels above the upper limits are increasingly associated with side effects.

**Classes of drug**

Digoxin may be given in a loading dose of 500–750 µg (0.5–0.75 mg) if fast action is necessary; 125–250 µg (0.125–0.25 mg) is the usual maintenance dose.

Digitoxin may be given in a loading dose of 300–400 µg (0.3–0.4 mg) daily for 3 days where needed, and 35–100 µg (0.035–0.1 mg) daily thereafter as the maintenance dose.

Ouabain, medigoxin and lanatoside C are alternatives still used in certain countries. They have no advantages over digoxin and digitoxin, and should no longer be used.

**Side effects**

Side effects are numerous and complex. Some, such as nausea and vomiting, may be less common in the elderly, while others, such as confusion, are certainly commoner. Side effects may be classified as follows.

Central nervous system side effects include nausea and vomiting, confusion, dizziness and rarely xanthopsia.

Cardiovascular side effects include bradycardia, ectopic beats and almost every arrhythmia, including fatal ventricular fibrillation. Where a cardiac arrhythmia is induced, cardiac glycosides should be withdrawn at once and serum potassium, creatinine and digoxin checked.

Other side effects include gynaecomastia.
Alternative drugs

Beta-blockers and verapamil may be useful in rapid ventricular rate in atrial fibrillation. Diuretics may be used as the sole treatment of cardiac failure, and are certainly effective. Inhibitors of angiotensin converting enzyme ("ACE inhibitors"), particularly enalapril, have gradually become drugs of first choice in the treatment of cardiac failure by virtue of their strong peripheral vasodilatory effect. Because of the risk of first-dose hypotension in the elderly, treatment should be started slowly, using low doses. Such treatment can, if necessary, be safely combined with cardiac glycosides and diuretics. The place of inotropic drugs other than digitalis glycosides is not yet firmly established.
Anti-arrhythmic drugs

Treatment of a cardiac arrhythmia requires a precise diagnosis, usually based on the demonstration of a temporal connection between an arrhythmic event and the patient’s symptoms (often necessitating 24-hour ECG monitoring). In patients with rapid ventricular rate in atrial fibrillation, thyrotoxicosis should first be ruled out.

Side effects with anti-arrhythmic drugs are common in the elderly, particularly with long-term use. Treatment should be restricted to patients with serious or debilitating symptoms due to arrhythmia and potentially life-threatening arrhythmias. Most anti-arrhythmics are myocardial depressants and can cause postural hypotension and heart failure. They may also interfere with the atrioventricular conduction system and thereby provoke life-threatening paradoxical ventricular tachyarrhythmias ("pro-arrhythmia").

Transitory tachycardias (e.g. atrial fibrillation and flutter) are commonly precipitated by chest infections or myocardial infarction in old people. Treatment should not be continued after the patient has reverted to normal sinus rhythm.

Cardiac arrhythmias in old age are often caused by drugs. Digitalis glycosides can produce virtually any disturbance of cardiac rhythm. Beta-blockers are often the culprit in sinus arrest, sinus bradycardia or atrioventricular block; even when given as eyedrops they can have this effect. Diuretic treatment may indirectly cause disturbances of heart rhythm by producing hypokalaemia or hypomagnesaemia. Erythromycin, sotalol, the tricyclic antidepressants in high dosage, some membrane-stabilizing neuroleptics (thioridazine) and some of the newer non-sedating antihistamines (terfenadine, astemizole) may also cause arrhythmias.

Indications and prescribing rules

The basic indication is a symptomatic arrhythmia. The following points should be noted.
Atrial fibrillation or flutter with rapid ventricular response should primarily be treated with digitalis glycosides (see page 64), monitoring the dosage according to the ventricular rate. In refractory cases thyrotoxicosis must be ruled out; these cases are usually managed by adding verapamil.

Atrial fibrillation or flutter with slow ventricular rate does not justify anti-arrhythmic treatment.

In paroxysmal atrial fibrillation, flutter and supraventricular tachycardia, the value of digitalis glycosides for prophylaxis is being questioned. If tolerated, verapamil, quinidine or disopyramide may be more effective alternatives.

In some cases paroxysmal atrial fibrillation is due to a “sick sinus” syndrome, which any antiarrhythmic drug is liable to worsen. Such cases often need a permanent pacemaker before effective anti-arrhythmic treatment of the tachycardia can be given.

Premature beats are usually asymptomatic in old people and should not be treated. In paroxysmal ventricular tachycardia, prophylaxis can be offered with mexiletine or propafenone. Drugs that induce pro-arrhythmia, such as quinidine or flecainide, should be avoided. Low-dose amiodarone is now widely used, but its many side effects make close observation of the patient mandatory.

Arrhythmias caused by digitalis intoxication are dealt with on page 69. Phenytoin and beta-blockers have some use in arrhythmias due to digitalis intoxication, where these need drug treatment.

Avoid combinations of two or more anti-arrhythmic agents (digitalis glycosides excepted) as this may induce severe heart block, myocardial failure or postural hypotension.

Be aware of the interaction propensities of anti-arrhythmics. When quinidine is given, it may be necessary to reduce the dose of digoxin or warfarin. Amiodarone and verapamil also reduce the clearance of digoxin and coumarin anticoagulants.
Most anti-arrhythmics are subject to quite marked variations in pharmacokinetics from person to person, which combined with their narrow safety margin (low therapeutic index) necessitates titration of the dosage. The routine determination of serum concentrations is therefore advisable for most anti-arrhythmics when used in old people.

**Classes of drug (for long-term use)**

**Membrane-stabilizing drugs (quinidine-like)**

*Usual oral dose in the elderly*

- mexiletine: 200 mg 3 times daily
- quinidine: 0.5–1.0 g twice daily (slow release)

Both drugs are useful in supraventricular as well as in ventricular forms of tachycardia. They have a vagolytic effect and, although they are usually prescribed with a cardiac glycoside for patients with rapid atrial fibrillation or flutter, this should be done with great care because of possible interaction between the drugs.

The most frequent side effects are postural hypotension, syncope, nausea, diarrhoea and allergic rash or thrombocytopenia. Quinidine-induced pro-arrhythmia seems to be more common than realized in the past.

**Beta-blockers** (see page 75)

These are effective in symptomatic tachycardias due to digitalis intoxication or thyrotoxicosis and in most supraventricular arrhythmias.

**Propafenone**

This drug combines anti-arrhythmic and beta-blocking properties. It is quite useful for the treatment of ventricular and
supraventricular arrhythmias, but it may aggravate existing atrio-
ventricular block. Because of its negative inotropic effect, it
should be used with caution in patients with a history of cardiac
failure. Dizziness is a common side effect. The starting dose
should not exceed 150 mg 3 times per day.

The beta-blocking drug sotalol has a similar bimodal mecha-
nism of action and a similar therapeutic profile.

Amiodarone

This very effective anti-arrhythmic drug can unfortunately elicit
a number of side effects, notably thyroid function changes (both
hypothyroidism and hyperthyroidism), pulmonary fibrosis and
hepatitis. It should be used only under strict cardiological su-
pervision, and doses should be kept as low as possible (daily
maintenance dose not exceeding 200 mg). Even so, it should be
reserved for the treatment of debilitating tachyarrhythmias in
pre-excitation syndromes.

Calcium antagonists (see verapamil, page 73)

Verapamil is very effective for the management of paroxysmal
supraventricular tachycardia, as well as atrial fibrillation and
flutter.

Cardiac glycosides (see page 64).
Drugs for angina pectoris

The diagnosis of angina pectoris is difficult in old age. Pain in the arms on exertion can be caused by arthritis, while post-prandial pain may be due to hiatus hernia, a frequent disorder in old age. Nocturnal angina can be mistaken for a peptic ulcer.

Angina in the elderly is often accompanied by dyspnoea. An accurate history and immediate relief by glyceryl trinitrate are the mainstays of diagnosis.

Adverse reactions to anti-anginal drugs are frequent and may interfere with compliance. All classes of anti-anginal drug can precipitate postural hypotension.

Overuse of glyceryl trinitrate can cause loss of efficacy (tolerance) and possibly also a rebound worsening of angina on sudden withdrawal.

Indications and prescribing rules

Ischaemic chest pain is frightening and incapacitating and should always be treated. Anti-anginal drugs (if necessary accompanied by reduction of weight, cessation of smoking and management of hypertension or cardiac failure) can be provided either for the acute treatment of the angina attack or as prophylaxis.

Acute attacks should be managed with glyceryl trinitrate sublingually at a low dosage to avoid light-headedness and a throbbing headache. Preferably a test dose should be given while a doctor or nurse is at hand.

Glyceryl trinitrate can be taken as an effective prophylactic agent immediately before strenuous exercise likely to precipitate pain (climbing stairs or hills, defecation, sexual intercourse).

Long-term prophylaxis should be provided if the patient experiences frequent attacks that interfere with normal activities or sleep. Beta-blockers, calcium antagonists or some long-acting nitrate preparations can be used, and the regimen should be tailored to the patient's needs.
Beta-blockers are especially suitable for angina on exertion in patients with hypertension, but may aggravate nocturnal angina. Beta-blockers cannot be used in patients with un-compensated heart failure and severe asthma.

Calcium antagonists (verapamil, nifedipine) are safe in the elderly and quite effective for angina on exertion, as well as nocturnal angina. They can be used by asthmatics, and precipitate heart failure only very rarely despite their being myocardial depressants. The calcium antagonist perhexiline is toxic and should not be used by old people. Calcium antagonists are contraindicated in patients with unstable (“pre-infarction”) angina.

Not all long-acting nitrate derivatives are well documented for the prophylaxis of angina pectoris, but isosorbide mononitrate and dinitrate are effective. Their anti-anginal effect is comparable to that of beta-blockers and calcium antagonists. Long-acting nitrates are safe for patients with heart failure and asthma. In order to prevent tolerance, however, slow-release preparations should only be given once daily, in the morning. Since these preparations may be ineffective in some patients, glyceryl trinitrate should not be withdrawn when they are prescribed.

**Classes of drug**

**Nitrate derivatives**

<table>
<thead>
<tr>
<th>Initial dose and usual dose in the elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>glyceryl trinitrate</td>
</tr>
</tbody>
</table>

If the first dose does not work, additional doses can be given at intervals of 5 minutes up to a total of 2–3 mg. Sustained unre-active pain may indicate myocardial infarction.
Oral glyceryl trinitrate slow-release tablets are not efficacious in the prophylaxis of angina (see above).

Glyceryl trinitrate preparations for transdermal application relieve anginal pain, but they are quite expensive and cumbersome to apply and remove. Too frequent use may induce nitrate tolerance and render the drug ineffective.

Glyceryl trinitrate given intravenously is very efficient in acute left heart failure with pulmonary oedema, but should not be given for ischaemic chest pain in old people, as severe hypotension can occur.

<table>
<thead>
<tr>
<th></th>
<th>Initial dose</th>
<th>Maximum dose in the elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>isosorbide dinitrate</td>
<td>5 mg 4 times daily</td>
<td>20 mg 4 times daily</td>
</tr>
<tr>
<td>isosorbide 5-mononitrate</td>
<td>10 mg twice daily</td>
<td>20 mg 3 times daily</td>
</tr>
<tr>
<td>isosorbide 5-mononitrate (slow-release)</td>
<td>60 mg in the morning</td>
<td></td>
</tr>
</tbody>
</table>

The most frequent side effects are postural hypotension and headache.

Under home conditions nitrate preparations often have a very limited life; a preparation more than two months old must be replaced. Tablets should not be removed unnecessarily from the original package.

**Beta-blockers** (see page 75).

**Calcium antagonists**

<table>
<thead>
<tr>
<th></th>
<th>Initial dose</th>
<th>Maximum dose in the elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>nifedipine</td>
<td>5 mg 3 times daily</td>
<td>10 mg 4 times daily</td>
</tr>
<tr>
<td>verapamil</td>
<td>40 mg 3 times daily</td>
<td>120 mg 3 times daily</td>
</tr>
<tr>
<td>diltiazem</td>
<td>60 mg 3 times daily</td>
<td>120 mg 3 times daily</td>
</tr>
</tbody>
</table>
The most frequent side effects are postural hypotension, headache and leg oedema, all probably due to vasodilation, and constipation. Calcium antagonists can precipitate left ventricular failure in patients with aortic stenosis.

Nifedipine and verapamil differ markedly. Verapamil counteracts atrioventricular conduction, making it a very useful anti-arrhythmic drug but precluding its use when atrioventricular conduction is disturbed; nifedipine does not have this effect. Where slow-release nifedipine is available, it may be found to be better tolerated by old people.
Beta-blockers

Beta-blockers are sometimes disappointing in old people, but where they prove effective they are still invaluable. Nevertheless, they are often overused in old people, being frequently prescribed for cardiovascular disorders for which they are only sporadically indicated.

Contraindications such as obliterating atherosclerosis, chronic airflow limitation and cardiac failure are often overlooked.

Minor adverse reactions are frequent, the most important in the elderly being postural hypotension, bradycardias (e.g. severe sinus bradycardia, sinus arrest and atrioventricular block), cardiac failure and asthma. There is often a sensation of coldness in the hands and feet. Neuropsychiatric disturbances can also occur.

Interpatient variations in pharmacokinetic parameters are marked for most beta-blockers, necessitating low initial dosage and careful titration of the dose for optimum efficacy and safety.

Abrupt withdrawal after prolonged use sometimes elicits a temporary state of adrenergic hypersensitivity with different forms of tachycardia, worsening of angina pectoris, or sudden death.

Beta-blockers, especially the alpha-/beta-blocker labetalol, can cause urinary incontinence.

Indications and prescribing rules

Angina pectoris on exertion in a hypertensive patient is the very best indication for a beta-blocker. Patients with nocturnal angina often deteriorate, as this condition may be related to left ventricular failure.

Essential tremor is sometimes improved by small doses of propranolol (10 mg 4 times per day). Beta-blockers are not much used for migraine in old people.
Beta-blockers have little use in tachycardias in the aged except in thyrotoxicosis. If beta-blockers are used as secondary prophylaxis after acute myocardial infarction after the age of 70, patients should be carefully monitored because of the relatively high incidence of adverse effects.

Timolol and betaxolol eyedrops are dealt with under Ophthalmological preparations (see page 131).

The initial dosage of a beta-blocker must be low. The dose should be titrated according to clinical efficacy and the occurrence of side effects (fatigue, cold hands and feet, dyspnoea). The antihypertensive effect may need 1–3 weeks to develop fully. Resting pulse rate should probably not be allowed to drop to under 45 beats per minute in old people. Blood pressure should be recorded sitting and standing.

If a beta-blocker is strongly indicated in a patient with mild chronic airflow limitation, one should apply a beta1-selective blocker and also prescribe a beta2-stimulator (e.g. salbutamol, terbutaline) to counteract bronchoconstriction. Even the beta1-selective blockers have some effect on the bronchial tree, and this can become clinically manifest at high dosage or in bronchitic exacerbations.

Remember that beta-blockers can mask the symptoms of hypoglycaemia in diabetics, in whom beta2-selective drugs are preferable.

Avoid fixed combinations of beta-blockers and diuretics. They may be convenient where it has first been shown that a patient needs both drugs in doses that correspond to those in a fixed combination, but in the elderly needs change as time passes.

Harmful interactions of beta-blockers with other drugs are shown in Table 7.

Avoid slow-release formulations of beta-blockers, which have been marketed in the hope of improving compliance. For angina pectoris and hypertension, which are the most common indications for beta-blockers in the elderly, dosage twice daily is sufficient for an optimum effect and dosage once daily does not improve compliance further. Moreover, slow-release tablets
are provided in one size only and are not supposed to be divided, thereby precluding the proper selection of the most suitable dosage.

Table 7. The potential consequences of interactions between beta-blockers and other drugs

<table>
<thead>
<tr>
<th>Interacting drug</th>
<th>Potential consequences</th>
</tr>
</thead>
<tbody>
<tr>
<td>verapamil</td>
<td>heart block, asystole, postural hypotension</td>
</tr>
<tr>
<td>disopyramide</td>
<td>heart failure, postural hypotension</td>
</tr>
<tr>
<td>nitrate derivatives</td>
<td>postural hypotension</td>
</tr>
<tr>
<td>sympathetic mimetic agents</td>
<td>reduction in antihypertensive effect</td>
</tr>
<tr>
<td>(e.g. in nasal drops)</td>
<td></td>
</tr>
</tbody>
</table>

Classes of drug

*Beta-blockers acting at both beta₁ and beta₂ adrenergic receptors (non-selective beta-blockers)*

<table>
<thead>
<tr>
<th>Initial dose</th>
<th>Maximum dose in the elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>propranolol</td>
<td>20 mg twice daily</td>
</tr>
<tr>
<td>sotalol</td>
<td>40 mg twice daily</td>
</tr>
</tbody>
</table>

Some of the older beta-blockers (e.g. alprenolol, oxprenolol and pindolol) possess a receptor-stimulating propensity (partial agonism, intrinsic sympathicomimetic effect). There is, however, no evidence that beta-blockers with partial agonist activity are more effective or better tolerated than others in the elderly.
**Beta-blockers acting predominantly at the beta<sub>1</sub>-adrenergic receptors (beta<sub>1</sub>-selective beta-blockers)**

<table>
<thead>
<tr>
<th></th>
<th>Initial dose</th>
<th>Maximum dose in the elderly</th>
</tr>
</thead>
<tbody>
<tr>
<td>atenolol</td>
<td>25 mg once daily</td>
<td>100 mg once daily (50 mg suffices in most cases)</td>
</tr>
<tr>
<td>metoprolol</td>
<td>25 mg twice daily</td>
<td>200 mg twice daily</td>
</tr>
</tbody>
</table>

These drugs have less effect on the beta<sub>2</sub>-receptors (in the bronchial tree and the peripheral vessels). The beta<sub>1</sub>-receptor selectivity of these drugs is not complete, however, and unwanted effects from beta<sub>2</sub>-receptor antagonism (asthma) can occur, e.g. at high doses.

The elimination of atenolol (and sotalol) depends on renal function. Dosage must be reduced in patients with renal failure.
Drugs for hypertension

Whether high blood pressure in the elderly should be aggressively treated is still highly controversial. Evidence from some large-scale trials has shown that treatment of mild hypertension in patients over the age of 65 does not prolong life or prevent major complications. At higher blood pressure levels, dietary salt restriction and thiazide diuretics are the mainstay of treatment; morbidity and mortality due to stroke are reduced, especially in female patients, whereas the effect on myocardial infarction is disappointing. Although there is still some doubt as to whether the hypotensive effect of beta-blocking agents is as good as that of diuretics, the former have been shown to reduce morbidity and mortality in elderly hypertensives as well as in elderly survivors of myocardial infarction. A beta-blocker, alone or combined with a thiazide diuretic, is particularly beneficial in those suffering from angina pectoris.

The use of calcium antagonists and ACE inhibitors has increasingly been advocated for some years. Although these drugs may have some theoretical advantages over older treatments, proof from large-scale trials of efficacy in the elderly is still lacking. The elimination of nifedipine is slowed down and acute sensitivity is enhanced; the initial dose should therefore be low and only very gradually increased. So far such problems have not been observed with the other dihydropyridine analogues or with verapamil or diltiazem. Most ACE inhibitors are excreted by the kidneys and the maintenance dose should therefore be carefully adjusted to renal function. Endogenous ACE activity in the elderly is reduced, but the hypotensive response to ACE inhibition may be abrupt and dramatic, causing tissue blood flow to fall below a critical threshold. In the renal and cerebral circulation this may cause irreversible ischaemic damage. There is a special indication for the use of ACE inhibitors in the treatment of hypertension in diabetic nephropathy.
A conservative approach towards the treatment of hypertension in old people seems therefore warranted. Only exceptionally should combinations of antihypertensive drugs be used, and preference is now given to single agents.

Classes of drug

*Diuretics*

The thiazide diuretics are to be preferred, and the dose should be as low as possible. Doses as low as 12.5 mg hydrochlorothiazide, 2.5 mg bendroflumethiazide or 25 mg chlortalidone per day are perfectly satisfactory, and potassium supplementation or the addition of potassium-sparing agents should not be necessary. Indapamide has no advantages over the other diuretics and, when used, the daily dose should not exceed 1.25 mg. Furosemide should not be used for the treatment of hypertension in the elderly because it has been associated with the occurrence of stroke.

Impotence is an unexpected but relatively common side effect of long-term thiazide treatment in elderly men.

*Beta-blockers*

The choice and dose are identical with those used in the treatment of angina pectoris (see page 75). The dose of atenolol should be decreased by 50% if creatinine clearance falls below 30 ml/min.

*Calcium antagonists*

All dihydropyridine analogues, with the possible exception of nifedipine, are safe and effective in the treatment of hypertension in the elderly and, taking body weight and kidney function into account, dosages and dosage schedules are the same as in younger people. Caution is necessary in patients with unstable
angina pectoris, and combination with other antihypertensive drugs should be avoided.

**ACE inhibitors**

Experience so far in large groups of old people is limited to captopril in low doses (25 mg twice a day or 12.5 mg 3 times a day) and to low-dose enalapril. More experience is needed to determine possible advantages or particular risks.

**Other antihypertensive drugs**

Many other drugs with vasodilatory properties, such as methyl-dopa, ketanserin, urapidil, prazosin and doxazosin, have been advocated for use in the elderly, but they are either less effective or carry particular risks. None has been studied for an appropriate length of time in elderly hypertensives, and their use can therefore not be recommended. Reserpine should no longer be used because it has no realistic safety margin when used in effective doses.
Lipid-lowering drugs

As in the treatment of hypertension, the goal of treatment with lipid-lowering drugs should not be the correction of a biochemical or clinical–physiological variable but the reduction of cardiovascular morbidity and mortality. It has been shown that high serum levels of cholesterol in people over 65 years of age are still a risk factor, but it has not yet been demonstrated that this will improve by simply lowering cholesterol values. The older drugs (nicotinic acid, fibrates) are relatively unsafe in the aged. If it is decided to give a drug, one of the HMG-CoA reductase inhibitors (i.e. lovastatin, simvastatin or pravastatin) is to be preferred, and the dose should be kept as low as possible.
Corticosteroids

Although corticosteroids are employed in the elderly for the same reasons as in the young, the elderly show a greater susceptibility to many side effects. Most of these are dose-related but some are irreversible. They include loss of bone substance with consequent vertebral and other fractures, hypertension, initiation or exacerbation of peptic ulcer, psychosis (whose minimum manifestations are insomnia, restlessness, euphoria and depression), the worsening of diabetes or a diabetic tendency, and reduced resistance to infections such as tuberculosis.

For these reasons corticosteroids should not be given to the elderly unless absolutely necessary.

Indications and prescribing rules

Short-term, high-dose treatment may occasionally be required – under very special circumstances – for severe infections and bacterial shock.

Long-term, high-dose therapy may be necessary for connective tissue diseases such as polymyalgia, giant cell arteritis, polymyositis, dermatomyositis, systemic lupus erythematosus and polyarteritis. Also in this group are autoimmune haemolytic anaemia, fibrosing alveolitis, and pemphigus and pemphigoid. Special high-dose treatment is necessary in space-occupying intracranial tumour. Head injuries and stroke do not respond.

Long-term, low-dose treatment may occasionally be helpful in airflow limitation shown to be responsive to corticosteroids, in rheumatoid arthritis, and as replacement therapy (with cortisone or fludrocortisone) in Addison’s disease and hypopituitarism.

Local therapy may be useful in the form of intra-articular injections in inflammatory arthritis, of steroid creams in eczematous conditions, of enemas in inflammatory bowel disease, of steroid eye drops in uveitis and of inhalations in asthma. Even here, adrenocortical suppression may occur.
Short-term, high-dose treatment consists of 60 mg prednisolone per day. The dose can safely be reduced in stages and finally stopped within 2 weeks or so.

Long-term, high-dose therapy consists of 7.5–10 mg prednisolone per day. High doses may be needed initially but should be reduced thereafter by gradual weekly decrements to the lowest dose possible for long-term treatment. In some cases (e.g. giant cell arteritis and polymyalgia) attempts to discontinue treatment should begin after a year, using the clinical state and the erythrocyte sedimentation rate as indicators. After long-term treatment, therapy should be withdrawn gradually.

Long-term, low-dose therapy consists of 2.5–7.5 mg prednisone per day. Here one should use the lowest possible dose that controls symptoms, with a temporary increase to 10 mg per day only to cover intercurrent illness and operations. Even with this type of therapy, drug withdrawal (where feasible) should be gradual.

Side effects

In all forms of steroid treatment the side effects listed above should always be watched for, and it may be necessary to discontinue treatment if they occur. Dose-related side effects will usually respond to a lowering of the dose or discontinuation of the drug. With other side effects it may nevertheless be necessary to persist with the treatment.

Alternatives to corticosteroids

There are many alternative and often safer treatments for individual diseases for which steroids are prescribed. These include non-steroidal anti-inflammatory drugs in joint disorders, aminosalicylic acid in colitis ulcerosa, and simple palliative creams and ointments in skin disorders.
Thyroid preparations

The diagnosis of hypothyroidism is difficult, and mild cases are easily missed unless specifically looked for.

Thyroid hormone administration can result in a dramatic improvement in patients with hypothyroidism. If too rapid, however, replacement therapy may precipitate myocardial ischaemia or cardiac failure. Start with the smallest possible dose and do not change the dosage at intervals of less than 1 week.

Another problem with replacement therapy is that patients, once they feel well, may stop taking their maintenance dose. Many apparently “new” cases in old age are known hypothyroid patients who have stopped treatment.

Indications and prescribing rules

Thyroid hormone is indicated:

- for replacement therapy in patients with hypothyroidism
- in some patients with goitre and thyroid carcinoma
- in combination with antithyroid drugs in patients with hyperthyroidism.

Use a modern preparation; thyroid extract should no longer be used since its effects are unpredictable.

Aim to restore and maintain normal levels of serum thyroxine and thyroid-stimulating hormone.

Ensure that patients understand that they have to take the thyroxine for the rest of their lives. Once well, patients may mistakenly think that they no longer require thyroxine.

Classes of drug

Levothyroxine (the levorotatory isomer of the natural thyroid hormone) is the treatment of choice. The starting dose in the
elderly is only 25 μg, increasing cautiously at monthly intervals. If no scored tablets of 50 μg are available, treatment on alternate days is feasible because of the long (3–5 days) duration of action. Liothyronine, a physiological precursor of thyroxine, is no longer used for substitution treatment because of its shorter half-life, unpredictable response and higher cost.
Antithyroid drugs

The first difficulty in the management of elderly patients with hyperthyroidism relates to the diagnosis. In the elderly many of the clinical manifestations may be less obvious and patients may present with cardiac features such as arrhythmia, often uncontrolled by digitalis.

Antithyroid drugs can effectively control the symptoms of hyperthyroidism. Once they are stopped, however, relapse is common. Too small a dose of an antithyroid drug may prove inadequate control, and too high a dose may result in hypothyroidism and an increase in the size of the goitre.

Antithyroid drugs

Indications and prescribing rules

Antithyroid drugs are indicated in the treatment of patients with hyperthyroidism, particularly where a rapid response is required. Start with a full dose. When the patient is euthyroid, usually after 4-8 weeks, reduce the dose to a maintenance level and continue for at least 18 months. When the patient is euthyroid, levothyroxine (50 µg per day) may be added to the antithyroid drugs to prevent the development of hypothyroidism.

When drugs are stopped, watch for a relapse of hyperthyroidism. Some workers have suggested the long-term administration of a small maintenance dose of an antithyroid drug in the elderly.

Classes of drug

Carbamazepine and propylthiouracil have the lowest reported incidence of side effects and are the drugs of first choice. If side effects develop with one drug, try a different drug. Cross-sensitivity between the thioureas and other drugs is uncommon.
Iodide as potassium iodide (30 mg 3 times daily) or as Lugol’s solution (0.1–0.3 ml 3 times daily) given for two weeks may be used to prepare patients for surgery or where a rapid control of symptoms is required.

Propranolol (40–200 mg 4 times daily) is useful where a rapid control of the clinical features is required or to control symptoms until other forms of therapy are effective. Table 8 summarizes the doses of antithyroid drugs. All act by blocking the synthesis of thyroid hormone.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Initial dose per day (mg)</th>
<th>Maintenance dose per day (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>carbimazole</td>
<td>20–60</td>
<td>5–15</td>
</tr>
<tr>
<td>thiamazole</td>
<td>15–60</td>
<td>5–30</td>
</tr>
<tr>
<td>propylthiouracil</td>
<td>300–600</td>
<td>50–300</td>
</tr>
<tr>
<td>methylthiouracil</td>
<td>400–600</td>
<td>200–300</td>
</tr>
</tbody>
</table>

**Alternative treatment**

Radioiodine therapy is the treatment of choice in the elderly. One regime combining radioiodine and antithyroid drug therapy is:

- give the prescribed dose of radioiodine;
- 4 days later, start antithyroid drugs;
  - after 1 month, add levothyroxine;
  - after 6 months, stop antithyroid drugs and levothyroxine and watch for the development of hypothyroidism or a recurrence of thyrotoxicosis;
  - if thyrotoxicosis recurs, prescribe a second dose of radioiodine.
All patients treated with radioiodine need to be assessed at yearly intervals because of the risk of developing hypothyroidism.

In the elderly, radioiodine or antithyroid drugs are usually preferable to surgery unless there is a large goitre.
Antimicrobial drugs

The use of these drugs in the elderly poses several problems and the clinician, in consultation with the patient or the family where appropriate, may come to the conclusion that no real benefit will be obtained from their use. Where benefit is possible, however, antimicrobial chemotherapy should be used.

The toxicity of antimicrobial drugs is an underestimated problem. Adverse drug reactions are common although many are only mild: for example, skin reactions are frequent. The aging ear labyrinth, kidney and liver do not take kindly to potent drugs. Ototoxic and nephrotoxic drugs such as the aminoglycosides should be avoided where possible or otherwise used in reduced dosage. Ideally, serum levels should be monitored. Tetracyclines raise blood urea and are dangerous in impaired renal function; doxycycline is safer but perhaps less effective except in bone infections.

This short section deals only with general principles.

Urinary tract infections

These are common. They often respond to co-trimoxazole, 2 tablets twice daily. Each of the standard tablets contains 80 mg (0.08 g) trimethoprim and 400 mg (0.4 g) sulfamethoxazole. In most uncomplicated infections trimethoprim alone should be used; the dose is 300 mg (0.3 g) daily or 200 mg (0.2 g) every 12 hours. Most side effects of co-trimoxazole are due to the sulfonamide component. Amoxicillin (500 mg (0.5 g) 3–4 times a day) is an alternative and better absorbed than ampicillin. Any of these drugs may cause headache, nausea, vomiting, diarrhoea, skin rashes or marrow depression. The skin rash of ampicillin may occur up to 2 weeks after the drug is stopped. While it does not indicate a general allergy for penicillin, it seems to be quite often associated with mononucleosis infections.

Catheter infections are difficult to treat. When a single organism is isolated on culture or (in the absence of culture
facilities) the patient has distress, drug therapy is needed. Bladder washouts with chlorhexidine may be of value. Some patients live in symbiosis with their catheter.

Nitrofurantoin and long-acting sulfonamides should not be used in the elderly.

**Chest infections**

As a rule these respond to the same drugs as urinary infections. Penicillin is still often the drug of choice. If these drugs fail, or if there is laboratory evidence or clinical suspicion of staphylococcal pneumonia, the drug of choice is a penicillinase-resistant penicillin. In the last resort one of the newer oral third-generation cephalosporins can be life-saving.

**Bowel infections**

Rehydration is essential.

Chemotherapy is not indicated except in: the enteric group of fevers (which respond to co-trimoxazole and chloramphenicol); *Campylobacter* enteritis (which responds to erythromycin and the fluoroquinolones); and giardiasis and *Entamoeba* infection (both of which respond to metronidazole).

**Gram-negative septicaemia**

This life-threatening situation is best treated with high intravenous doses of an “anti-*Pseudomonas*” penicillin such as piperacillin or ticarcillin, a cephalosporin, gentamicin or kanamycin (the last two being ototoxic as well as nephrotoxic). Sometimes corticosteroids and pressor agents may be required.

**Virus infections**

Idoxuridine, applied locally, is of some use in treating zoster shingles. Amantadine has also been used. None of the systemic
antiviral drugs is of much proven value, although aciclovir or vidarabine can be useful in very early zoster.

**Tuberculosis**

Tuberculosis is normally initially treated with a triple regime, e.g. including 450 mg rifampicin before breakfast (600 mg if the patient is over 50 kg in weight), ethambutol in a daily dose of 15 mg per kg body weight, and isoniazid (300 mg daily); later a two-drug regime can be used.
Anti-arthritic drugs

There are many causes of arthritis in the elderly and a proper diagnosis must be made.

The large number of non-steroidal anti-inflammatory drugs (NSAID) available makes rational selection difficult. Many can cause serious interactions with drugs such as the coumarin anticoagulants.

All NSAID cause gastrointestinal disturbances including bleeding, probably in proportion to their anti-inflammatory activity, and many cause fluid retention or interfere with neurological function.

Old people are at particular risk from the side effects of corticosteroids, gold preparations and penicillamine.

Indications and prescribing rules

In long-standing symptomatic rheumatoid arthritis, pain is often due to secondary osteoarthritis rather than synovial inflammation.

Rheumatoid arthritis of recent onset is often particularly acute in old people and associated with systemic disturbances. The long-term prognosis is good.

For osteoarthritis, hydroxyapatite crystals may cause considerable inflammation, so that NSAID are often better than simple analgesics.

Start off with a simple analgesic such as paracetamol. If this proves ineffective, switch to an NSAID of low toxicity (ibuprofen or naproxen). Where the condition is osteoarthritic, little anti-inflammatory activity is needed, so the more active and toxic compounds can usually be avoided.

Use a drug that can be given twice (or even once) rather than 3–4 times daily.

Continue with treatment for at least 3 weeks at the optimal dosage before changing.
If one of the NSAID is ineffective, switch to another rather than continuing with two preparations. Since there are unpredictable individual differences in response to particular NSAID, even where they are very similar, try at least four such drugs in succession before going on to other forms of pharmacological treatment.

If pain is not relieved by an NSAID alone, it is worth adding a simple analgesic such as paracetamol.

Doctors should familiarize themselves with four NSAID and use other agents only in exceptional circumstances.

Use penicillamine or gold only if:

- there is clinical or laboratory evidence of soft tissue inflammation;
- pain is not relieved by NSAID;
- treatment is likely to improve the capacity for self-care; or
- the disease has systemic manifestations.

Ensure that these drugs are prescribed in containers that even arthritic hands can open.

Avoid the temptation to switch to a newly introduced drug unless the patient has real problems with the existing therapy; new anti-arthritic drugs are usually no better, and some have caused severe toxicity problems in the elderly.

Do not use an expensive NSAID in rheumatoid arthritis if a cheap one is just as good.

**Classes of drug**

**NSAID**

**Salicylates**

These are extremely effective, but often cause nausea, vomiting, diarrhoea or gastrointestinal haemorrhage. Old people are
particularly likely to suffer from tinnitus, dizziness or even deafness. Gastrointestinal disturbance may sometimes be reduced by using buffered, micro-encapsulated and enteric coated preparations.

_Pyrazoles_

Phenylbutazone and azapropazone may cause severe gastric irritation, fluid retention or aplastic anaemia and should not be used in the elderly.

_Indoles and related compounds_

Indometacin is effective but also causes gastric irritation and fluid retention. Headache, drowsiness and confusion may also occur in old people.

Sulindac is similar but rather less likely to cause gastric upsets and has a long half-life. The dose is one or two 100-mg tablets twice daily.

_Propionic acid derivatives_

These are less likely to cause gastric damage than aspirin or indometacin. Fenbufen and naproxen have long half-lives so that they need only be given once or twice daily.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>naproxen</td>
<td>250–500 mg twice</td>
</tr>
<tr>
<td>ibuprofen</td>
<td>200–400 mg 3 times (maximum 2.4 g daily)</td>
</tr>
<tr>
<td>fenprofen</td>
<td>300–600 mg 3 times (maximum 3 g daily)</td>
</tr>
<tr>
<td>ketoprofen</td>
<td>50 mg 2–4 times</td>
</tr>
<tr>
<td>flurbiprofen</td>
<td>50–150 mg 3 times</td>
</tr>
<tr>
<td>fenbufen</td>
<td>300–450 mg twice</td>
</tr>
</tbody>
</table>
Fenamates

These often cause diarrhoea in old people, and can produce severe dehydration. Examples are mefenamic acid and flufenamic acid. The former at least can cause renal failure, diarrhoea and sometimes haemolytic anaemia.

Other classes of NSAID

Piroxicam has a different structure from other NSAID, but its efficacy is similar to that of the propionic acid derivatives. The dose is 10–20 mg given only once daily, which is a minor advantage. It is more likely, however, to cause gastrointestinal irritation, ulceration and haemorrhage, especially in the elderly.

Second-line drugs

Gold

This is effective in active rheumatoid arthritis. Serious side effects include skin rashes, bone marrow suppression and renal damage. The risk can be minimized by regularly checking full blood counts and the urine for protein.

Sodium aurothiomalate is given by intramuscular injection, 50 mg per week for 20 weeks, carefully monitoring for side effects and discontinuing if these occur.

Penicillamine

This acts similarly to gold. The starting dose is 125–250 mg daily, increasing cautiously to not more than 500 mg daily in old people. Avoid its use in renal and hepatic disease and look out for proteinuria. A loss of taste may occur for some weeks; rashes are common and some are persistent.
Corticosteroids

These should be used for the treatment of rheumatoid arthritis in old age only if the condition is acute and of recent onset.

Alternatives to drugs

Drugs are often complementary to other forms of therapy; in severe painful arthritis of the hip, replacement of the hip joint is likely to be needed.
Muscle relaxants

Not all stiffness in old people is spasticity. It is important to distinguish between stiffness due to fixed contractures and cogwheel rigidity due to parkinsonism.

In old people, spasticity is usually associated with a hemiparesis complicating a cerebrovascular accident. The key to prevention and treatment is to start physiotherapy on the affected limbs as soon as possible after the stroke. Training by the physiotherapist should be reinforced by efforts on the part of the nursing staff, relatives and the patient. Muscle relaxant drugs are no substitute for this. The relief of spasticity with drugs may sometimes increase disability. For example, a spastic extended knee is more useful than one that is flaccid and flexed. Most muscle relaxants have a more general effect on the central nervous system. The cost of a reduction in tone may be drowsiness, confusion or ataxia.

Indications and prescribing rules

The valid indications are

- spastic flexion of an elbow interfering with dressing
- spastic plantar flexion of a foot reducing mobility
- spastic deformity, e.g. knee flexion, making nursing more difficult.

Muscle relaxants have a very limited use; they should be used only as an adjunct to physiotherapy. Start off with a small dose, increasing this every few days until the drug relieves the symptoms or side effects become intolerable.
Classes of drug

Centrally acting agents

Diazepam

Despite the fact that many doctors use oral diazepam in muscle spasticity, there is no firm evidence that it works. Old people are particularly susceptible to the central effects of benzodiazepines, so that drowsiness, confusion, or disinhibition and inappropriate behaviour are common even with relatively small doses.

Diazepam may be given orally before a physiotherapy session to facilitate limb movement. Dangers are that the patient may sleep through the session, or fall and fracture a hip.

Peripherally acting agents

Baclofen

This agent has a direct effect on afferent–efferent synapses for motor units within the spinal cord. It is useful in the management of spasticity associated with spinal cord damage, but requires more detailed evaluation in spasticity resulting from stroke.

In old people the starting oral dose should be 5 mg daily, increasing every few days to a maximum of 100 mg in divided doses.

Drowsiness, ataxia and nausea are common. Old people often experience mood changes, or may become confused or have hallucinations.

Tizanidine

The mode of action and the side effects of this drug are largely similar to those of baclofen. Experience in the elderly is still limited. The starting and maintenance dose is 6–12 mg daily.
Dantrolene

Dantrolene reduces tone by interfering with calcium metabolism in the sacroplasmic reticulum of skeletal muscle. It has been used widely in the management of spasticity due to lesions of the spinal cord and the cerebral cortex.

The starting oral dose is 25 mg daily, increasing over 7 weeks to a maximum of 100 mg 4 times daily. If the drug has no effect after 45 days, it should be stopped.

Despite its peripheral site of action, dantrolene may cause drowsiness, dizziness, weakness or fatigue. One in two hundred patients develops drug-induced hepatitis; the regular monitoring of liver function tests is therefore important.
Drugs used in gout

High serum uric acid levels are common in old age, and are sometimes the result of diuretic therapy. They occasionally cause acute attacks of gout.

Old people are at particular risk from the side effects of drugs used to treat an acute attack of gout.

Indications and prescribing rules

An acute attack of gout has to be treated. Where attacks are frequent, maintenance therapy is required.

An acute attack of gout is of such severity that even in old age the primary considerations should be the efficacy of treatment rather than potential side effects. Treatment should, therefore, be started with the most effective drug in the most effective dose. The risk of side effects will be reduced if the dosage is decreased and stopped as soon as symptoms have subsided.

The treatment of an acute attack of gout associated with myeloproliferative disorders (see page 133) is the same as that for other forms of the condition. Such attacks should be followed by prophylaxis in all cases.

A high serum uric acid level should be left untreated if it is not associated with symptoms.

Drugs that reduce the serum uric acid may themselves precipitate an acute attack of gout.

Classes of drug

Non-steroidal anti-inflammatory drugs

Indometacin

This is given in an oral dose of 50 mg 4 times daily until the joint pain settles. The dosage is then progressively reduced and discontinued over the course of 2 days. It may cause
gastrointestinal damage and fluid retention. Side effects include headache, drowsiness, mental confusion and depression.

Naproxen

This is given in a 750-mg (0.75-g) dose followed by 250 mg (0.25 g) every 8 hours, decreasing as symptoms allow. Adverse effects resemble those of indomethacin.

Colchicine

Colchicine has a large number of serious side effects, notably severe diarrhoea, but is effective in the treatment of acute attacks of gout. The initial dose is 1 mg, followed by 0.5 mg each hour up to a maximum of 8 mg.

Prophylactic agents

Allopurinol

This inhibits the formation of uric acid from xanthine. The starting dose is 100 mg daily, increasing weekly to a maximum of 300 mg daily, depending on serum uric acid levels. The more common side effects are skin rashes and gastrointestinal upsets.

Probenecid

This increases the urinary excretion of uric acid. Since this increases the risk of calculus formation, the drug has taken second place to allopurinol in the control of serum uric acid levels. The dosage is 250 mg (0.25 g) twice daily, gradually increasing to 1 g twice daily if necessary, depending on serum uric acid levels.
Analgesics

Pain is a subjective phenomenon related to a wide range of factors, including boredom and depression.

In patients with malignancy, pain is not always due to the tumour. It may be the result of a pressure sore, osteoarthritis or cystitis.

Patients may develop tachyphylaxis to analgesics so that even large doses are ineffective.

Pain may be relieved at the expense of clouding of consciousness.

Narcotic drugs have serious side effects that include vomiting, constipation and respiratory depression.

Old people may be hypersensitive to narcotics and lose consciousness on a dose recommended for young adults.

Addiction is not a problem in the treatment of terminal illness. A more common problem is dependency on drugs such as dihydrocodeine or dextropropoxyphene when they are used inappropriately in old people.

Indications and prescribing rules

Find out the cause of a pain before resorting to analgesics. A headache associated with a cerebral tumour responds better to corticosteroids than to morphine. Carbamazepine is of specific value in trigeminal neuralgia. Phenol nerve block is of value in intransigent regional pain such as that due to metastases. Neuroleptics may be a valuable supplement to analgesics in severe pain but may cloud consciousness. Tricyclic antidepressants can help to relieve pain, even in non-depressed patients.

Treat the patient and not the pain alone. Explanation and reassurance may be as important as the analgesic.

Give analgesics to a patient frequently and regularly rather than on demand. Start with a small dose and rapidly increase this until the pain is controlled. Patients treated in this way
require smaller doses, and are rarely troubled by clouding of consciousness.

Anticipate the side effects of morphine by using anti-emetics and laxatives where appropriate.

In terminal illness the dose of analgesic should be sufficient to relieve pain even if, in extreme cases, this shortens the patient’s life expectancy. There is no maximum dose.

Consider the use of salicylates in pain due to skeletal metastasis. Non-steroidal anti-inflammatory drugs (NSAID) act in this situation by suppressing prostaglandin synthesis.

In minor illnesses avoid analgesics likely to produce dependency.

Avoid combinations of analgesics when prescribing for minor symptoms.

Classes of preparation

Paracetamol

This analgesic is the drug of choice in the control of minor pain. It has no anti-inflammatory effects and may not be sufficient in severe pain, but, since it has few side effects, old people should be encouraged to take this, rather than salicylates, when resorting to self-medication. The dose is 0.5–1 g, up to a maximum of 4 g in 24 hours. Combination preparations of paracetamol and aspirin with or without codeine or caffeine should be avoided, because their misuse by elderly women is a contributory cause of renal failure (“analgesic nephropathy”).

Ibuprofen

This weak member of the NSAID group is now widely used in low (200 mg) doses as an alternative to paracetamol or aspirin. It has no particular advantages over these and, when dosage recommendations are exceeded, it causes dyspepsia and acute renal insufficiency in rare cases. It should not be used by patients with a history of peptic ulcer.
**Codeine and dihydrocodeine**

These opiates have a potency similar to that of paracetamol, but they may cause severe constipation. They should be used with some caution in old people. Combinations with paracetamol or aspirin enjoy some popularity, but they are only marginally better than the single drug and less safe.

**Dextropropoxyphene with paracetamol (Distalgesic)**

Where available this combination is popular with old people, possibly because it has a euphoriant effect. Some patients, however, develop dependence and withdrawal sometimes produces psychotic symptoms. Overdosage, especially in combination with overuse of alcohol, carries a high risk of death. Remember that dextropropoxyphene is akin to the opiates.

**Pentazocine and pethidine**

These opioid drugs have only a weak analgesic effect when taken orally. They may cause confusion and should not be given to old people.

**Morphine**

This is widely used in the management of pain in terminal illness, for which it is usually prepared as an elixir with or without chlorpromazine, depending on whether the patient has nausea. Dosage should start at 5 mg every 4 hours, gradually increasing to a maximum of 100 mg every 4 hours or until the pain is relieved. If the dose is increased in this way, patients can tolerate massive quantities and remain alert. Nausea and cholinergic side effects can to some extent be prevented by the addition of atropine (0.25 mg atropine to 10 mg morphine).

Oral slow-release formulations of morphine have become very useful alternatives for the treatment of cancer pain, making it
possible to reduce the frequency with which the drug has to be given.

**Methadone, buprenorphine and butorphanol**

Though pharmacologically more potent, all three are equivalent to morphine but have a longer half-life. Repeated dosage may result in cumulation. They should be used in old people only if, for some reason, morphine is unacceptable. Experience with these drugs in the elderly is limited. All are addictive.

A wide range of other narcotic analgesics is available, but these offer no clear advantage over morphine in the management of terminal illness in old people.
Anticonvulsants

Epileptic seizures are not rare in the elderly, but neither are the side effects of anticonvulsants. Particular difficulties result from the persistence of focal signs for two or three days or more (Todd’s paralysis, or perhaps recovery from drugs given for the seizure). These may be mistaken for strokes and may give rise to concern that the cause of the fits is, for instance, an intracranial tumour.

Bear in mind that alcohol withdrawal (e.g. for medical reasons) is an occasional cause of convulsions; these are best treated with a parenteral benzodiazepine and prophylaxis with anticonvulsants is not indicated.

Indications and prescribing rules

The indications for anticonvulsant therapy are two or more properly diagnosed epileptic seizures. It is doubtful whether one or more seizures occurring during an acute illness that resolves should necessitate anticonvulsant therapy for the rest of the patient’s life. Prophylactic drug therapy may be necessary after head injury and intracranial operations.

Phenytoin, carbamazepine or sodium valproate are much to be preferred to phenobarbital in the elderly when new patients are treated.

A single drug regime is to be preferred to multiple drugs, but these may be needed in resistant cases.

Measurement of serum concentrations is valuable, although the therapeutic range is less clearly defined in the elderly than in the young.

If no seizure occurs for 3 years, drug therapy may be cautiously reduced and withdrawn. In about 50% of patients fits do not recur after drug withdrawal.
Classes of drug

Phenytoin

Phenytoin is given in an initial dose of 200 mg per day and a maximum single daily dose of 300 mg. This produces usually therapeutic drug levels of 10–20 μg/ml (20–40 μmol/ml) and avoids toxicity, which is increasingly encountered at higher levels. Drowsiness, nystagmus, ataxia, falls, abnormal movements, occasionally a drug rash or fever, and a lymphoma-like syndrome are all seen as toxic effects. In patients on long-term treatment, folate deficiency and perhaps osteomalacia need to be considered and regular monitoring, probably every 6 months, is necessary.

Carbamazepine

Patients who are too heavily sedated with phenytoin can be controlled with carbamazepine, an alternative first-line drug. The daily dose varies considerably (up to 1.2 g per day) and that needed to produce serum levels in the therapeutic range of 5–10 μg/ml (20–40 μmol/ml) should be found. Dose-related side effects include drowsiness, nystagmus and hyponatraemia; skin rashes and aplastic anaemia also occur, although rarely.

Sodium valproate

Sodium valproate is effective in absences (almost unknown in the elderly) but less so in grand mal seizures and ineffective in partial seizures. Coated tablets are available in some countries and seem to be better tolerated. The dosage should be 200–500 mg 3 times a day. In grand mal seizures the drug may be given in 200-mg doses up to 6 times a day.
Other preparations

Other anticonvulsants are rarely needed or used in the elderly, but intravenous or rectal diazepam or clonazepam are of value in status epilepticus.
Antiparkinson drugs

The proper treatment of Parkinson's disease depends on an accurate diagnosis (the presence of bradykinesia and rigidity, with or without typical tremor) and an assessment of disability and its mechanisms. Many cases are drug-induced, particularly by phenothiazines and butyrophenones, and an accurate history of drug use must always be taken; these forms of parkinsonism may take up to 2 years to disappear after the offending drug has been discontinued. Other disease processes (notably dementia and depression) may greatly affect the patient's disability, and must be taken into account when this is assessed.

Indications and prescribing rules

The indication for drug treatment is not the diagnosis itself, or tremor alone, but a significant degree of disability due to parkinsonism. Rigidity and bradykinesia are the principal mechanisms that produce disability.

Treatment should not be started until parkinsonism is producing disability. In the elderly this is most often at the time of diagnosis and there is no place for delaying treatment when it is necessary.

Bear in mind that antiparkinson drugs as a group create problems for the patient, and every effort must be made to individualize treatment so as to ensure that the adverse effects are not disproportionate to the benefit obtained.

It is preferable not to withdraw drugs when admitting patients to hospital.

Classes of drug

Levodopa

Levodopa may be better absorbed in the elderly than in the young (probably because of reduced gastric dopamine decarboxylase)
but is now rarely given alone. The two combination forms of levodopa with a decarboxylase inhibitor, i.e. carbidopa or benserazide, should be given initially in small doses (62.5 mg 1–3 times per day) with a gradual increase at intervals of not less than 5–7 days. The average maximum dose in elderly patients is approximately 750–1000 mg (0.75–1 g) of levodopa (as Sinemet or Madopar). Once a patient is controlled, adverse effects may sometimes be lessened by cautious reduction of the dosage and the use of small doses at shorter intervals.

Adverse reactions and the effects of overdosage include confusion, psychosis, involuntary movements, nausea and postural hypotension. The fear of cardiac arrhythmias is unwarranted, but a watch should be kept on patients with severe heart disease for the development of cardiac failure associated with increased activity resulting from the successful treatment of parkinsonism.

**Anticholinergic drugs**

Anticholinergic drugs have largely been superseded, and they should not normally be prescribed for new patients. They may, however, be given to elderly patients with disability due to tremor that is unrelieved by levodopa, or for troublesome salivation. They should not be used routinely in elderly patients as prophylaxis for parkinsonism when psychotrophic drugs liable to induce parkinsonism are being given.

Orphenadrine (50–150 mg per day), biperiden (2–6 mg per day) and trihexyphenidyl (2–6 mg per day) are the most used. Side effects are frequent and include, in particular, aggravation of urinary retention, constipation, glaucoma and confusion.

**Bromocriptine**

This is an alternative or addition to levodopa, especially useful when the use of levodopa raises problems. Special indications include loss of effect of levodopa in adequate doses, and uncontrollable swings of parkinsonism. It should be given in a
manner similar to levodopa, i.e. in small doses building up to approximately 15 mg per day. Its side effects resemble those of levodopa; nausea, dyskinetic movements and psychosis are the most important and frequent.

**Other drugs**

Other drugs, such as selegiline, pergolide and lisuride, have been little tried in the elderly. Although there is some evidence that selegiline given in an early stage postpones the moment that levodopa treatment has to be started, there is as yet no irrefutable evidence that this is also the case in the aged. Amantadine has little place, as its effectiveness is limited to a few months at the most; the side effects resemble those of levodopa. Since it is excreted by the kidney, smaller doses are required in the elderly.

**Alternatives to drugs**

There is no fully effective alternative treatment to drugs, but these may not completely abolish long-term disability. The place of physiotherapy is uncertain, but the occupational therapist can be of great value in rearranging the patient's activities and in providing aids to daily living. Speech therapy has a definite place in the management of the common speech disorder of Parkinson's disease, if this is causing disability.

**Treatment of tardive dyskinesias**

These can arise as a complication of the prolonged use of neuroleptics or related drugs (e.g. some antihistamines, metoclopramide, domperidone) or spontaneously. Mild cases, without serious physical or social consequences, are probably best left untreated. Response to treatment is often incomplete. Anticholinergic drugs may cause further deterioration of the mental state of the patient, and if possible their use for this purpose should be avoided.
Dyskinesia may occur after a neuroleptic is withdrawn, and in such cases the drug may have to be restarted in low doses.
Drugs for disturbed behaviour

Disturbed behaviour is a symptom. Before any drug is considered, the cause of the symptom must be discovered. Full physical examination before drug medication is essential. Treatment of acute or long-standing undiagnosed physical disease will often relieve all behavioural disturbance. Cessation of all medication, with few exceptions, enables a clearer view to be taken of the patient’s condition.

Correct patient management is the primary key to the treatment of these patients; drug treatment is ancillary and can even worsen confusion.

Progressive vascular occlusions affecting the brain may cause only intermittent behavioural disturbance.

Medication should be timed to cover expected problems such as evening restlessness or wandering.

The treatment of depressive features, anxiety and restlessness evident in dementing patients is necessary, as is treatment of any coincidental conditions.

A review of the patient’s social condition is essential; its improvement may make drug treatment unnecessary.

Indications and prescribing rules

An acutely disturbed, aggressive patient may initially need a powerful tranquillizer to allow full physical examination. Continuous restlessness and wandering should be controlled by appropriate doses of a less potent neuroleptic such as thioridazine.

Depression must always be treated.

Use the appropriate drug for the diagnosed condition.

Drugs should be given in doses worked out individually for each patient to obtain the desired effect. Patients should not be tranquillized into complete immobility.

Fluid preparations are often more appropriate and more certain to be swallowed.
Patients who refuse medication will often accept the treatment if it is re-presented after an interval. Remember the hangover effects, which may be prolonged if hypnotics are prescribed. Restrict prescribing to a minimum number of drugs and become familiar with their effects.

**Classes of drug**

**Neuroleptics (major tranquillizers)**

The various types of neuroleptic vary in their potency but not greatly in their spectrum of activity. Side effects include parkinsonism, tardive dyskinesia, sudden falls and hypotension; temperature control can be deranged. Chlorpromazine is more prone than other neuroleptics to produce jaundice. Patients on tranquillizers must be encouraged to drink extra fluids.

**Chlorpromazine**

Powerful neuroleptics such as chlorpromazine should be used in old people only when absolutely necessary. A single intramuscular injection will allow initial examination. Chlorpromazine should preferably not be used for long-term tranquilization.

**Thioridazine**

Long-term major tranquilization can be managed by individually measured doses of a less potent drug such as thioridazine. Thioridazine can be given in small doses during the day (e.g. 10 mg 3 times daily) and in a larger dose (50–100 mg) in the evening to act as a hypnotic.

**Haloperidol**

Noisy restlessness responds to haloperidol, the dose of which can be individually measured to control the patient; this drug can be combined with food, as it is tasteless.
Anxiolytics (see page 17).

Hypnotics (see page 117).

Antidepressants (see page 120).

**Drugs to delay or reverse progressive brain failure**

These have yet to be discovered; all claims to the contrary can be safely ignored. Even the controversial and potentially dangerous new drug tacrine has so far not reached this goal. Proof of efficacy for any of the so-called “cerebral vasodilators” is lacking.
Hypnotics and anxiolytics

With advancing age the duration of sleep tends to decrease and the pattern of sleep to alter. The elderly often complain of insomnia, but the particular causes of insomnia should be sought before a hypnotic is prescribed.

Anxiety is a normal response to stress and only when it is severe and disabling should it lead to drug treatment. Long-term treatment with anxiolytics and hypnotics is rarely effective and should be avoided.

Most hypnotic and anxiolytic drugs belong to the same family (the benzodiazepines). The elderly tend to be more sensitive to the effects of these drugs and their elimination may be impaired. Side effects are therefore more common, particularly hangover effects with hypnotics and cumulation with anxiolytics. The other important problems are tolerance, dependence and paradoxical withdrawal effects when these drugs are abruptly stopped. Both classes of drugs are much overused in the elderly, especially in institutions, and, once started, therapy may all too easily be continued for long periods in the absence of any need.

Indications and prescribing rules

Hypnotics and anxiolytics are needed when sleeplessness or anxiety have no evident or curable cause and are severe enough to cause a real problem, such as chronic tiredness or impaired function.

Give anxiolytics and hypnotics only for as long as they are needed, then stop.

Because of increased sensitivity and impaired elimination, the elderly need smaller doses than the young. Hangover effects and cumulation can be avoided by using drugs with appropriately short durations of action, and short-term use (less than 2 weeks) will minimize the risk of dependence. Awareness of
these potential problems and a high level of suspicion should help to avoid unnecessary morbidity.

Bear in mind that both hypnotics and anxiolytics are markedly potentiated by alcohol.

Few patients need both an anxiolytic and a hypnotic; the combination readily results in over-sedation.

Classes of drug

Hypnotics

Benzodiazepines

These are effective hypnotics and extremely safe. They do cause dependence but this is generally less marked than with any other effective hypnotic. About 20 different benzodiazepines are now marketed throughout the world. For the elderly the shorter-acting ones, such as triazolam (dose 0.125–0.25 mg (125–250 µg)) are in theory better, but they may cause rebound daytime phenomena including increased anxiety. Intermediate-acting agents with simple elimination pathways such as oxazepam or temazepam (each at a dose of 10–20 mg) may be preferable. Where cost is important, one of the older members of the group such as nitrazepam (dose 2.5–5 mg) may suffice, provided that hangover effects are watched for. Flurazepam is not recommended for use in elderly patients owing to a high incidence of adverse effects, particularly at higher doses.

Chloral hydrate

This is effective and may be cheaper than benzodiazepines, but it is far less safe and causes more side effects. The elixir is unpalatable and its smell on the patient’s breath may be socially unacceptable.

Anxiolytics

There is little to choose between the benzodiazepines marketed for the treatment of anxiety and cost may be the deciding factor.

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The dose should be less than the usual adult dose and cumula-
tion should be watched for.

There are really no suitable alternatives to the benzodiazepines for the treatment of anxiety. Barbiturates should not be used for the treatment of either anxiety or sleep disorders because they are less safe than the benzodiazepines.

**Side effects**

Look out particularly for over-sedation, ataxia and sudden falls. Nightmares and hallucinations are rare, but withdrawal effects may occur even after a few days on a normal dose.

**Combinations**

It is rarely necessary to combine benzodiazepines with other types of psychotropic medication. If insomnia and anxiety accompany depression, a sedative antidepressant such as amitriptyline will usually prove effective.

**Alternatives to drugs**

Discussion of the problems of sleeplessness and anxiety and the drawbacks of drug therapy will often help the patient to come to terms with his or her problem without the need to resort to drugs. Noise, pain and stimulant drinks or drugs at bedtime or late in the day should be dealt with appropriately.

Depression or other primary problems should be treated appropriately, and this will often result in improvement of sleep or relief of anxiety, without the need for hypnotic or anxiolytic drugs.
Antidepressants

Depression is the commonest psychiatric disorder in the elderly and is often associated with physical disease, bereavement or an adverse environment. It may also accompany other conditions such as dementia and may be induced by treatment with drugs.

While diagnosis is similar to that in younger age groups, it is often made more difficult by the presence of other illness and by old age itself.

With all types of antidepressant agent there is some increase in side effects in the elderly and this, together with the diagnostic complications, may make the decision to treat more difficult. The choice of individual agent and of dose may also be more difficult than in younger patients.

Compliance may be a problem in long-term therapy.

Some drugs, such as reserpine given for hypertension, are a notorious cause of depression in the elderly.

Indications and prescribing rules

Antidepressant therapy is often beneficial in the elderly, both in simple depressive states and when associated with anxiety or psychosis. Drug therapy is indicated in most cases where depressive symptoms fail to improve with supportive measures.

In cases of severe depression in elderly patients, the risk of suicide should be constantly kept in mind.

Owing to increased sensitivity to side effects and in some cases impaired elimination, the elderly need smaller doses than the young – often a third to a half of the standard adult dose – although there is considerable individual variation in dose requirements. In some cases a single dose at night may produce fewer side effects than divided doses. Where there are suicidal tendencies, small drug quantities should be prescribed, and supervision of drug dosing is necessary in depression associated with dementia.
The onset of beneficial effects may take 2–3 weeks and, where benefit is obtained, treatment should be continued for several months. In general, owing to increased sensitivity to drug side effects, combinations of agents are not advised in the treatment of depressive states in the elderly. Where depression is associated with anxiety, a “sedative” antidepressant is preferable to the additional prescribing of a benzodiazepine. In cases of gross agitation, addition of a phenothiazine may prove useful, particularly where a “sedative” antidepressant has proved ineffective.

**Classes of drug**

**Tricyclic drugs**

The tricyclic agents (e.g. amitriptyline, imipramine, nortriptyline, clomipramine) are effective antidepressants in the elderly, but adverse anticholinergic effects (constipation, glaucoma, blurred vision, difficulty in micturition, dry mouth) and cardiovascular effects (postural hypotension) may occur. They should be used with care in patients with a history of cardiac disease. Drowsiness may also be a problem but, anxiety or agitation often being part of the clinical picture, the sedative effects of amitriptyline (25–50 mg daily in divided doses or as a single night dose) may be used to advantage. Imipramine (10–75 mg daily) produces less sedation. There is little pharmacokinetic justification for the use of long-acting preparations of tricyclic agents.

**Modified tricyclic drugs**

There is little evidence for any increase in efficacy with the newer agents (e.g. doxepin, maprotiline) but side effects seem to be less common. Maprotiline is initially given in 3 doses of 10 mg or as a single dose of 30 mg at bedtime, and can be increased gradually as necessary to a maximum of 150 mg daily.
Non-tricyclic drugs

Mianserin (30–60 mg at night) is in general well tolerated in elderly patients and the complications of overdosage are possibly less severe. In view of the risk of agranulocytosis developing during the first few weeks of treatment, regular white cell counts are recommended.

Monoamine oxidase inhibitors

Monoamine oxidase inhibitors may be considered in situations where other antidepressant agents have proved ineffective and the patient can be relied on to follow the necessary dietary advice. They must be used with caution in older people, however, since they have a particular propensity for producing interactions and adverse effects. The hypertensive attacks that readily occur if the patient also takes sympathicomimetic drugs or tyramine (e.g. in cheese) are notorious. These drugs should be used only on specialized psychiatric advice.

Serotonin uptake inhibitors

The safety profile of these drugs (fluoxetine, fluvoxamine, sertraline) in the elderly seems to be quite favourable, but in this age group they seem to be less effective than the tricyclic antidepressants. Their excitatory and sleep-inhibiting effects make them unsuitable for agitated patients or elderly people with sleeping disorders.

Lithium salts

Lithium salts may be used, though with great caution, in some depressive states in the elderly. They are particularly effective in depressive states associated with agitation. The half-life of lithium is prolonged when renal clearance is reduced (as in many old people) and careful dosing, with monitoring of plasma
concentration (therapeutic range 0.5–1 mmol/l) is essential. Overdosage may cause irreversible renal or cerebral damage.

Alternatives to drugs

In minor depressive illness, and particularly in situational depression, environmental improvements – simple support and social contact – may be sufficient. In severe depression, particularly with suicidal tendencies, or in depression that fails to respond to drug treatment, electroconvulsive therapy should be considered as a means of producing more rapid improvement.
Cerebral vasodilators and activators

There is little valid evidence that the intracranial arteries of the elderly are capable of dilatation, except under the influence of carbon dioxide. There is even less evidence that, if vasodilation does occur, it is of benefit.

Many drugs that were at first promoted as cerebral vasodilators are now promoted as cerebral activators. For some of these there is certain suggestive evidence that is claimed to support their use, but there have been problems in the appropriate selection of patients for the studies concerned and the effects obtained are generally of little significance for daily life. All of these drugs cause side effects. Naftidrofuryl may cause headache, abdominal pain, diarrhoea and nausea. Cyclandelate may cause nausea and flushing. Co-derecine can cause nausea, visual upsets, skin rashes, bradycardia and nasal stuffiness. Other products with emphatic claims include the “nootropic” drug piracetam, the central stimulants meclofenoxate and pyritinol, and the xanthine derivative pentoxifylline.

Despite the very widespread use of such drugs, they cannot be considered to be of any benefit, except perhaps very occasionally; these drugs are expensive and toxic, and therefore should not be used as placebos.
Anti-obesity drugs

Appetite suppressants are rarely indicated and should not be used in the elderly, principally because they are ineffective except in producing side effects on the central nervous system. Thyroid hormones should certainly never be used to reduce weight. Moreover, the widely used amphetamine-like drugs fenfluramine and its dextrorotary isomer dexfenfluramine may in rare cases cause irreversible pulmonary hypertension. Bulking agents (see page 125) are of some limited use and do no harm.

The alternative is careful adherence to a weight-reducing diet and sufficient physical exercise.
Bronchodilators

Bronchodilators should be given for reversible bronchoconstriction, and their effectiveness should be monitored in terms of improvement not only in the patient’s symptoms but in specific tests for airflow limitation (e.g. peak flow rate or forced expiratory volume). They should not be given if they are demonstrably ineffective in the latter sense. Infection may need to be treated with antibiotics; it should be diagnosed at least by inspection of the sputum.

Alternatives include systemic steroid therapy and cessation of cigarette smoking. The former may be dangerous, and the latter very difficult.

Classes of drug

Adrenergic agonists

Salbutamol and terbutaline may cause confusion and tremor in high doses. Both can be given orally, or preferably by inhalation (as aerosol or powder). The elderly may have considerable difficulty in using inhalers correctly and must be actively instructed. Nebulized inhalation enhances drug delivery. Inhalation therapy should preferably be restricted to the treatment of acute symptoms (“on demand”); whether continuous treatment with some of the newer long-acting sympathicomimetics is preferable and safe enough is still being discussed. Fenoterol has been associated with death from acute asthma in New Zealand. Combinations of these drugs with anticholinergics offer no clinically relevant advantages over single preparations.

The maximum oral dose of both terbutaline and salbutamol should be 10 mg per day.
**Xanthines**

*Theophylline*

This should preferably be given as a slow-release anhydrous preparation (60–250 mg (0.06–0.25 g) 3–4 times daily). It can also be used intravenously in emergencies (250–500 mg (0.25–0.5 g) or 5 mg per kg body weight, slowly, in the form of aminophylline). High blood levels can cause nausea and vomiting, cardiac arrhythmias and confusion. Aminophylline should never be given intramuscularly, as it is very painful and can cause abscesses. In long-term treatment, blood levels should be checked regularly and kept between 5 and 20 mg/l. Theophylline is no longer regarded as the mainstay of asthma treatment.

**Other drugs**

*Sodium cromoglycate*

This has been little tried in elderly patients but is apparently rarely effective, perhaps because elderly patients only rarely suffer from a type of asthma likely to respond.

**Inhaled corticosteroid preparations**

These (beclometasone and budesonide) have rapidly gained in popularity. They involve compliance problems and may result in fungal infections of the mouth, pharynx and bronchi. These aerosols may be difficult to handle for many elderly patients, and they may induce fungal infections of the oropharynx. This complication may be largely prevented by washing the oral cavity with water after inhalation. High doses are partially absorbed and may suppress cortisol production in the adrenals.
Cough suppressants

A cough is a symptom of underlying disease, and suppression may obscure the diagnosis. For example, a dry, non-productive cough may be the first sign of tuberculosis.

Suppression of cough in chronic bronchitis is positively harmful, leading to the cumulation of secretions in the bronchi. Many suppressants also depress the respiratory centre, so that blood carbon dioxide concentrations rise with further depression of respiration.

Most cough suppressants interfere with colonic motility, leading to constipation.

Some prescribing rules

Identify the cause of a cough wherever possible.

If the cough is troublesome but non-productive and not associated with serious pathology, give a mild cough suppressant.

If the cough is the result of pulmonary malignancy use a more potent suppressant.

Most cough suppressants are available in simple liquid forms such as linctus. These are usually preferable since they are easier to take than tablets and improve the degree of subjective relief. Complex mixtures should be avoided.

Classes of drug

Mild cough suppressants

Codeine is used orally in a dose of 15–30 mg.

Noscapine is a cough suppressant derived from an opium alkaloid that, within the therapeutic range, has little effect on the respiratory centre. The dose is 15–30 mg 3–4 times per day. It is of uncertain value, but appears to ease a cough if not to suppress it.
Expectorants

No expectorant or mucolytic agent seems likely to be more effective than a glass of warm water. In patients with dryness and irritation of the respiratory passages it is important to maintain adequate hydration. The inhalation of steam gives some relief from the symptoms.
Antihistamines

Antihistamines are rarely indicated in the elderly except for genuine histamine-related allergic phenomena, and as sedatives. Antihistamines are ineffective for dizziness and should therefore not be used.

For alternatives, see under Hypnotics, page 118.
Ophthalmological preparations

Most of these should be prescribed for an older patient only on the advice of an ophthalmologist. Some systemic drugs have prominent ophthalmic side effects (e.g. precipitation of narrow angle glaucoma by any drug with anticholinergic effects).

**Systemic preparations**

Short-term, high-dose or long-term high-dose corticosteroids (see page 83) may be needed for giant-cell arteritis to prevent blindness.

Acetazolamide (a carbonic anhydrase inhibitor and weak diuretic) may still be used in the treatment of glaucoma.

**Local preparations**

**Drugs acting on the pupils**

**Dilators**

Homatropine methylbromide eyedrops may be used after cataract surgery for retinal examination.

**Constrictors**

Pilocarpine or epinephrine eyedrops are used to control the intraocular pressure in glaucoma.

**Beta-blockers**

Timolol and betaxolol eyedrops are effective in the treatment of raised intraocular pressure, but systemic absorption occurs and can be associated with the side effects of beta-blockade, including precipitation of asthmatic attacks and cardiovascular effects.
Other agents

Neomycin and bacitracin eyedrops
These are used in the treatment of microbial conjunctival infections; they are of no value when the conjunctivitis has another cause.

Artificial tear products
These are useful for dryness of the eye (e.g. Sjögren’s syndrome).

Chloramphenicol eyedrops
These should not be used, since even by this route the drug can cause blood dyscrasias.

Sulfonamide eyedrops
These may actually cause or activate conjunctivitis.

Corticosteroid eyedrops
These should be avoided wherever possible because of the grave risk of corneal perforation.
Drug treatment of malignant blood disorders

The modern treatment of leukaemia is of considerable complexity, and elderly patients with acute leukaemia are best treated by specialists. Symptoms are usually present in chronic myeloid leukaemia and it should be treated. Chronic lymphatic leukaemia, however, is often asymptomatic in the elderly and should be treated only if there is significant anaemia (which is often haemolytic), thrombocytopenia, large gland masses or constitutional symptoms. Myeloma should be treated whether there are symptoms or not, since its development may be prevented by relatively simple chemotherapy.

Acute leukaemia

Treatment should often be symptomatic and supportive only, as the prognosis in the elderly is usually to be measured in weeks. A generally fit person should be given combination chemotherapy for the most usual myeloblastic form of the disease.

Chronic myeloid leukaemia

Chronic myeloid leukaemia should be treated with hydroxy-carbamide (40–80 mg per day) until the white cell count has been reduced to 20 000/mm$^3$ or the platelet count to 10 000/mm$^3$. When the platelet level reaches its nadir, dosage should be reduced until the level stays around 25 000/mm$^3$. The drug is then continued in a lower dose sufficient to maintain the white cell count at the same level. Irreversible bone marrow damage may follow excessive dosage. The second-line drug is oral busulfan in a dose of 4–6 mg per day; pigmentation, anorexia and sometimes pulmonary fibrosis may result from long-term administration.
Chronic lymphatic leukaemia

The asymptomatic patient is best left untreated. If serious symptoms occur, chlorambucil is given in a dose of 0.1–0.2 mg (100–200 μg) per kg body weight, and this will result in lowering of the white cell count and reduction in the size of gland masses. After approximately 1 month the dose should be reduced to that needed to control the white cell count. Corticosteroids may be necessary if haemolysis is a major cause of anaemia.

Myeloma

The therapy currently advised is a combination of melphalan (0.25 mg (250 μg) per kg body weight every day) and prednisone (60 mg per day) in courses of 4 days every 4–6 weeks according to the blood count. Treatment should continue until the white cell count or the platelet count reaches dangerous levels, or until symptoms are controlled. Blood transfusions are likely to be needed.

Polycythaemia vera

This is treated by venesection to reduce the haematocrit; the patient may thereafter be treated with chlorambucil.
Drug treatment of malignant disease

The common malignant diseases of old age should receive other than supportive treatment only if they are giving rise to symptoms or are highly likely to do so. For instance, carcinoma of the lung should be treated with radiotherapy (and rarely with chemotherapy) only if there is pain from rib involvement, or if the tumour is in the right upper lobe and superior mediastinal obstruction is therefore likely. Non-metastatic metabolic complications such as hypercalcaemia may require treatment (e.g. with steroids) in their own right, with much benefit. Otherwise simple symptomatic treatment, for instance with antimicrobials for respiratory infection, has been shown to give an equal duration and quality of life to that produced by radiotherapy.

Somewhat similar considerations apply to gastrointestinal malignant disease, which requires surgical treatment if it is causing obstruction but not if lymph node or hepatic metastases are causing few or no symptoms. Cytotoxic therapy is usually more beneficial to the relatives and the doctor than to the patient, and generally should not be used. If doses sufficient to control symptoms resulting from malignant disease are given, symptoms due directly to the treatment are very frequent and it is doubtful whether the quality of the patient’s life is improved.

Specific drug treatment of two common cancers, those of the prostate and the breast, should be considered.

Primary carcinoma of the prostate

Early localized cancers often remain asymptomatic for many years, and do not really benefit from estrogen therapy. In the later stages of the disease, however, with gland masses in the pelvis and elsewhere, or bone or bone marrow involvement, estrogen therapy gives symptomatic relief. Diethylstilbestrol
(1–5 mg per day) may be given, though it is no longer available in some countries. Metastatic masses may shrink, bone pain may be relieved, and leuko-erythroblastic anaemia may be controlled. The quality of life, if not its length, may be much improved. More recently, anti-androgens such as flutamide and agents that stimulate the continuous production of luteinizing hormone releasing hormone (LHRH agonists) have been shown to provide striking relief without the undesirable effects of estrogen therapy or orchidectomy.

**Carcinoma of the breast**

This may be treated by operation, particularly if local ulceration is present or imminent. Metastatic disease, commonly that of bone, should be treated with tamoxifen (20 mg per day), which is particularly effective in the elderly. There appears to be no particular advantage in other forms of drug therapy in the elderly. In advanced cases patients are commonly treated with combinations of cytostatic drugs in order to relieve bone pain and other debilitating symptoms.

**Malignant blood disorders** (see page 133).
Oxygen therapy may save life in reversible hypoxia due, for example, to airflow limitation pneumonia and pulmonary congestion or oedema. It is, however, of no clear value unless the pO$_2$ is below 55 mmHg. Danger exists in patients with chronic hypoxia, where often the respiratory centre is no longer driven by rising levels of carbon dioxide but by oxygen lack. In these patients intemperate use of oxygen can lead to death from respiratory arrest. Such high-risk patients should be given low-concentration controlled oxygen (24–30%) using nasal catheters or a Ventimask or Edinburgh mask. Such methods may be used at home but are very expensive. Many elderly people find all forms of oxygen administration intolerable. The oxygen tent is almost obsolete.

When oxygen is essential, great care must be taken with refrigeration or warming, depending on the ambient temperature.

When oxygen therapy is used, except for very short periods, care must be exercised with regard to humidification. Water vapour with a particle size of 7 μm is vital to prevent laryngotracheobronchitis.

Monitoring of pCO$_2$ and pO$_2$ is highly desirable.
Annex 1

Recommended sources of information and suggestions for further reading

Books


Reviews


Index of drug names appearing in the monographs

Names in bold type are those of drugs appearing in the eighth list of the WHO Model List of Essential Drugs¹

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General prescribing rules for the elderly

1. Think about the necessity for drugs. Is the diagnosis correct and complete? Is drug therapy really necessary? Is there a better alternative?
2. Do not prescribe drugs that are not useful. Think carefully before giving old people drugs that may have major side effects and consider alternatives.
3. Think about the drug dose. Is it appropriate to possible alterations in the patient's physiological state? Is it appropriate to the patient's renal and hepatic function at the time?
4. Think about drug formulation. Is a tablet the most appropriate form of drug, or would an injection, a suppository or a syrup be better? Is the drug suitably packaged for elderly patients, bearing in mind their disabilities?
5. Assume that any new symptoms may be due to drug side effects, or more rarely to drug withdrawal. Rarely (if ever) treat a side effect of one drug with another.
6. Take a careful drug history. Bear in mind the possibility of interaction with substances that the patient may be taking without your knowledge, such as herbal or other non-prescribed remedies, old drugs taken from the medicine cabinet or drugs obtained from friends.
7. Use fixed combinations of drugs only when they are logical and well studied and they either aid compliance or improve tolerance or efficacy. Few fixed combinations meet this standard.
8. When adding a new drug to the therapeutic regimen, see whether another can be withdrawn.
9. Attempt to check whether the patient's compliance is adequate, e.g. by counting remaining tablets. Has the patient (or his or her relatives) been properly instructed?
10. Remember that stopping a drug is as important as starting it.