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 indometacin.

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 corticocosteroids 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 psychotropic 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 tranquillization.

Thioridazine

Long-term major tranquillization 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 drug 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.

The dose should be less than the usual adult dose and cumulation 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-dergocrine 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 dextrorotatory 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 hydroxycarbamide (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

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

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STAESSEN, J. ET AL. Relation between mortality and treated blood pressure in elderly patients with hypertension. *British medical journal*, **298**: 1552–1555 (1989).

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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 Drugs[1]

[1] *The use of essential drugs. Sixth report of the WHO Expert Committee.* Geneva, World Health Organization, 1995 (WHO Technical Report Series, No. 850), pp. 60–63.

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.

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