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 atrioventricular 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 mechanism 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 supervision, 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 uncompensated 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

	Initial dose and usual dose in the elderly
glyceryl trinitrate	0.25–0.5 mg

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 unreactive 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.

	Initial dose	*Maximum dose in the elderly*
isosorbide dinitrate	5 mg 4 times daily	20 mg 4 times daily
isosorbide 5-mononitrate	10 mg twice daily	20 mg 3 times daily
isosorbide 5-mononitrate (slow-release)	60 mg in the morning	

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

	Initial dose	*Maximum dose in the elderly*
nifedipine	5 mg 3 times daily	10 mg 4 times daily
verapamil	40 mg 3 times daily	120 mg 3 times daily
diltiazem	60 mg 3 times daily	120 mg 3 times daily

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 antiarrhythmic 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 $beta_1$-selective blocker and also prescribe a $beta_2$-stimulator (e.g. salbutamol, terbutaline) to counteract bronchoconstriction. Even the $beta_1$-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 $beta_1$-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

Interacting drug	Potential consequences
verapamil	heart block, asystole, postural hypotension
disopyramide	heart failure, postural hypotension
nitrate derivatives	postural hypotension
sympathicomimetic agents (e.g. in nasal drops)	reduction in antihypertensive effect

Classes of drug

Beta-blockers acting at both beta$_1$- and beta$_2$-adrenergic receptors (non-selective beta-blockers)

	Initial dose	*Maximum dose in the elderly*
propranolol	20 mg twice daily	120 mg twice daily
sotalol	40 mg twice daily	160 mg twice daily (with specific anti-arrhythmic activity)

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 $beta_1$-adrenergic receptors ($beta_1$-selective beta-blockers)

	Initial dose	*Maximum dose in the elderly*
atenolol	25 mg once daily	100 mg once daily (50 mg suffices in most cases)
metoprolol	25 mg twice daily	200 mg twice daily

These drugs have less effect on the $beta_2$-receptors (in the bronchial tree and the peripheral vessels). The $beta_1$-receptor selectivity of these drugs is not complete, however, and unwanted effects from $beta_2$-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 methyldopa, 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 eyedrops 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 atrial fibrillation, often uncontrolled by digitalis.

Antithyroid drugs can effectively control the features of thyrotoxicosis. Once they are stopped, however, relapse is common.

Too small a dose of an antithyroid drug may give inadequate control, and too high a dose may result in hypothyroidism and an increase in the size of the goitre.

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 thyrotoxicosis. Some workers have suggested the long-term administration of a small maintenance dose of an antithyroid drug in the elderly to prevent a relapse.

Classes of drug

Carbimazole and propylthiouracil have the lowest reported incidence of side effects and are the drugs of first choice.

Antithyroid drugs are in general well tolerated, but side effects such as drug rashes or agranulocytosis are not uncommon.

If side effects develop to one drug, try a different drug. Cross-sensitivity between the thiouracils 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 8. Doses of antithyroid drugs

Drug	Initial dose per day (mg)	Maintenance dose per day (mg)
carbimazole	20–60	5–15
thiamazole	15–60	5–30
propylthiouracil	300–600	50–300
methylthiouracil	400–600	200–300

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.

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.

	Daily dose
naproxen	250–500 mg twice
ibuprofen	200–400 mg 3 times (maximum 2.4 g daily)
fenoprofen	300–600 mg 3 times (maximum 3 g daily)
ketoprofen	50 mg 2–4 times
flurbiprofen	50–150 mg 3 times
fenbufen	300–450 mg twice

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 cog-wheel 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.