

# Drug Monographs

## 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

#### *Nonspecific 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<sub>2</sub>-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 H<sub>2</sub>-receptor antagonist or omeprazole should be used.

### ***Benign stricture of the oesophagus***

There is no evidence that histamine H<sub>2</sub>-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 H<sub>2</sub>-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 H<sub>2</sub>-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 H<sub>2</sub>-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 H<sub>2</sub>-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 H<sub>2</sub>-receptor antagonists. It has proven to be particularly effective for the treatment of reflux oesophagitis, but has no advantages over histamine H<sub>2</sub>-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.

|                    | <i>Form</i>                | <i>Daily dose at bedtime</i> |
|--------------------|----------------------------|------------------------------|
| senna              | tablets, granules or syrup | 7.5–30 mg                    |
| bisacodyl          | coated tablets             | 2↔5 mg                       |
| sodium picosulfate | elixir or enema            | 5–15 ml                      |

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 terodiline 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  $\alpha_1$ -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 5. Classes and doses of sulfonylurea

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

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

Table 6. Varieties of insulin

| Variety                                | Peak action (hours) | Duration of action (hours) |
|--|---------------------|----------------------------|
| Short-acting<br>soluble                | 2-4                 | 6-12                       |
| Intermediate<br>isophane insulin       | 5-12                | 12-25                      |
| insulin zinc<br>suspension (amorphous) | 3-6                 | 12-16                      |
| Long-acting<br>protamine zinc          | 5-14                | 24-30                      |
| Combinations<br>short + intermediate   | 2-10                | 18-20                      |
| insulin zinc suspension                | 3-8                 | 16-24                      |

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.

## 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 formes frustes are 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.

|                                | <i>Calcium per tablet</i> | <i>Daily dose</i> |
|--------------------------------|---------------------------|-------------------|
| calcium gluconate              | 600 mg                    | 2 tablets         |
| calcium gluconate effervescent | 400 mg                    | 3 tablets         |

### ***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 alfacalcidol***

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- $\beta$ -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- $\beta$ -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 dextrans 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*

|              |   |
|--------------|---|
| therapeutic  | 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 |
| prophylactic | 5000 i.u. 2 or 3 times daily subcutaneously   |

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*

(doses indicated are for warfarin)

|                  |   |
|------------------|---|
| initial doses    | 5–10 mg on day 1, slightly less on day 2          |
| maintenance dose | up to 10 mg daily according to laboratory control |

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, gastro-intestinal haemorrhages can be precipitated, so this prophylaxis is not suitable for a patient with a peptic ulcer or symptomatic hiatus hernia.

### ***Dextrans***

Dextrans 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. Dextrans should not be given in impaired renal function.

No laboratory control is necessary when dextrans 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 B<sub>12</sub> 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 B<sub>12</sub> 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 B<sub>12</sub> 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 B<sub>12</sub>***

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  $140 \mu\text{mol/l}$  ( $1.58 \text{ mg/100 ml}$ ), doses of  $250 \mu\text{g}$  ( $0.25 \text{ mg}$ ) per day of digoxin are correct; if levels are higher than these,  $125 \mu\text{g}$  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.