above

Dose: by mouth, 2.5 g initially, followed by 3 further doses of 2.5 g every 4 hours

Methionine (Non-proprietary)

Tablets, DL-methionine 250 mg. Net price course of 40 tabs = £12.27

Available from Norton

ANALGESICS (OPIOID)

Opioids (narcotic analgesics) cause varying degrees of coma, respiratory depression, and pinpoint pupils. The specific antidote **naloxone** is indicated if there is coma or bradypnoea. Since naloxone has a shorter duration of action than many opioids, close monitoring and repeated injections are necessary according to the respiratory rate and depth of coma. Alternatively, it may be given by continuous intravenous infusion, the rate of administration being adjusted according to response.

CO-PROXAMOL. Combinations of dextropropoxyphene and paracetamol (co-proxamol) are frequently taken in overdosage. The initial features are those of acute opioid overdosage with coma, respiratory depression, and pinpoint pupils. Patients may die of acute cardiovascular collapse before reaching hospital (particularly if alcohol has also been consumed) unless adequately resuscitated or given **naloxone** as antidote to the dextropropoxyphene. Paracetamol hepatotoxicity may develop later and should be anticipated and treated as indicated above.

NALOXONE HYDROCHLORIDE

Indications: overdosage with opioids; for postoperative respiratory depression, see section 15.1.7

Cautions: physical dependence on opioids; cardiac irritability; naloxone is short-acting, see notes above

Dose: by intravenous injection, 0.8–2 mg repeated at intervals of 2–3 minutes to a max. of 10 mg if respiratory function does not improve (then question diagnosis); CHILD 10 micrograms/kg; subsequent dose of 100 micrograms/kg if no response

By subcutaneous or intramuscular injection, as intravenous injection but only if intravenous route not feasible (onset of action slower)

By continuous intravenous infusion, 2 mg diluted in 500 mL intravenous infusion solution at a rate adjusted according to the response

IMPORTANT. Doses used in acute opioid overdosage may not be appropriate for the management of opioid-induced respiratory depression and sedation in those receiving palliative care and in chronic opioid use, see also section 15.1.7 for management of postoperative respiratory depression

syringe = £5.25, 2-mL disposable syringe = £9.74

PoM **Narcan®** (Du Pont)

Injection, naloxone hydrochloride 400 micrograms/mL, net price 1-mL amp = £4.79

Neonatal preparations —section 15.1.7

ANTIDEPRESSANTS

Tricyclic and related antidepressants cause dry mouth, coma of varying degree, hypotension, hypothermia, hyperreflexia, extensor plantar responses, convulsions, respiratory failure, cardiac conduction defects, and arrhythmias. Dilated pupils and urinary retention also occur. Metabolic acidosis may complicate severe poisoning; delirium with confusion, agitation, and visual and auditory hallucinations, is common during recovery.

Symptomatic treatment and activated charcoal by mouth may reasonably be given in the home before transfer but hospital admission is strongly advised, and supportive measures to ensure a patent airway and adequate ventilation during transfer are mandatory. Intravenous diazepam may be required for control of convulsions (preferably in emulsion form). Although arrhythmias are worrying, some will respond to correction of hypoxia and acidosis; the use of anti-arrhythmic drugs is best avoided. Diazepam given by mouth is usually adequate to sedate delirious patients but large doses may be required.

ANTIMALARIALS

Overdosage with chloroquine and hydroxychloroquine is extremely hazardous and difficult to treat. Urgent advice from a poisons information centre is essential. Life-threatening features include arrhythmias (which can have a very rapid onset) and convulsions (which can be intractable). Quinine overdosage is also a severe hazard and calls for urgent advice from a poisons information centre.

BETA-BLOCKERS

Therapeutic overdosages with beta-blockers may cause lightheadedness, dizziness, and possibly syncope due to impaired circulation secondary to bradycardia and hypotension; heart failure may be precipitated or exacerbated. These complications are most likely in patients with pre-existing conduction system disorders or impaired myocardial function. Bradycardia is the most common arrhythmia caused by beta-blockers, but sotalol occasionally induces ventricular tachyarrhythmias (sometimes of the torsades de pointes type). The effects of massive overdosage may vary from one beta-blocker to another; propranolol overdosage in particular may cause coma and convulsions.

Acute massive overdosage must be managed in hospital and expert advice should be obtained. Maintenance of a clear airway and adequate ventilating). A further dose of glucagon (or an intravenous infusion) may be required if the response is not maintained. If glucagon is not available, intravenous isoprenaline or intravenous prenalterol [not on UK market] are alternatives to glucagon.

HYPNOTICS AND ANXIOLYTICS

BARBITURATES. These cause drowsiness, coma, respiratory depression, hypotension, and hypothermia. The duration and depth of cerebral depression vary greatly with the drug, the dose, and the tolerance of the patient. The severity of poisoning is often greater with a large dose of barbiturate hypnotics than with the longer-acting phenobarbitone. The majority of patients survive with supportive measures alone. Charcoal haemoperfusion is the treatment of choice for the small minority of patients with very severe barbiturate poisoning who fail to improve, or who deteriorate despite good supportive care.

BENZODIAZEPINES. Benzodiazepines taken alone cause drowsiness, ataxia, dysarthria, and occasionally minor and short-lived depression of consciousness. They potentiate the effects of other central nervous system depressants taken concomitantly. Flumazenil, a benzodiazepine antagonist, may be used in the *differential diagnosis* of unclear cases of multiple drug overdose but expert advice is **essential** since adverse effects may occur (e.g. convulsions in patients dependent on benzodiazepines).

IRON SALTS

Iron poisoning is commonest in childhood and is usually accidental. The symptoms are nausea, vomiting, abdominal pain, diarrhoea, haematemesis, and rectal bleeding. Hypotension, coma, and hepatocellular necrosis occur later. Mortality is reduced with intensive and specific therapy with **desferrioxamine**, which chelates iron. The stomach should be emptied at once by gastric lavage. The serum-iron concentration is measured as an emergency and intravenous desferrioxamine given to chelate absorbed iron in excess of the expected iron binding capacity. In **severe toxicity** intravenous desferrioxamine should be given *immediately* without waiting for the result of the serum-iron measurement (contact a poisons information centre for advice).

DESFERRIOXAMINE MESYLATE

(Deferoxamine Mesilate)

Indications: removal of iron from the body in poisoning; for use in chronic iron overload, see section 9.1.3

Cautions: avoid prochlorperazine

amine mesylate. Net price 500-mg vial = £3.70

LITHIUM

Most cases of lithium intoxication occur as a complication of long-term therapy and are caused by reduced excretion of the drug due to a variety of factors including dehydration, deterioration of renal function, infections, and co-administration of diuretics or NSAIDs (or other drugs that interact). Acute deliberate overdoses may also occur with delayed onset of symptoms (12 hours or more) due to slow entry of lithium into the tissues and continuing absorption from modified-release formulations.

The early clinical features are non-specific and may include apathy and restlessness which could be confused with mental changes due to the patient's depressive illness. Vomiting, diarrhoea, ataxia, weakness, dysarthria, muscle twitching, and tremor may follow. Severe poisoning is associated with convulsions, coma, renal failure, electrolyte imbalance, dehydration, and hypotension.

Therapeutic lithium concentrations are within the range of 0.4–1.0 mmol/litre; concentrations in excess of 2.0 mmol/litre are usually associated with serious toxicity and such cases may need treatment with haemodialysis (if there is renal failure). In acute overdosage much higher serum concentrations may be present without features of toxicity and measures to increase urine production are usually all that are necessary. Otherwise treatment is supportive with special regard to electrolyte balance, renal function, and control of convulsions.

PHENOTHIAZINES AND RELATED DRUGS

Phenothiazines cause less depression of consciousness and respiration than other sedatives. Hypotension, hypothermia, sinus tachycardia, and arrhythmias (particularly with thioridazine) may complicate poisoning. Dystonic reactions can occur with therapeutic doses, (particularly with prochlorperazine and trifluoperazine) and convulsions may occur in severe cases. Arrhythmias may respond to correction of hypoxia and acidosis but anti-arrhythmic drugs may also be needed. Dystonic reactions are rapidly abolished by injection of drugs such as benztropine or procyclidine (see section 4.9.2).

STIMULANTS

AMPHETAMINES. These cause wakefulness, excessive activity, paranoia, hallucinations, and hypertension followed by exhaustion, convulsions, hyperthermia, and coma. The early stages can be controlled by chlorpromazine and, if necessary, beta-blockers. Later, tepid sponging, anticonvulsants, and artificial respiration may be needed. Amphetamine excretion can be increased by forced acid diuresis but this is seldom necessary.

multiple drugs for their multiple diseases. This greatly increases the risk of drug interactions as well as other adverse reactions. Moreover, symptoms such as headache, sleeplessness, and lightheadedness which may be associated with social stress, as in widowhood, loneliness, and family dispersal can lead to further prescribing, especially of psychotropics. The use of drugs in such cases can at best be a poor substitute for effective social measures and at worst pose a serious threat from adverse reactions.

FORM OF MEDICINE. Elderly patients may have difficulty swallowing tablets; if left in the mouth, ulceration may develop. They should always be encouraged to take their tablets or capsules with enough fluid, and in some cases it may be advisable to prescribe liquid if available.

MANIFESTATIONS OF AGEING. In very old subjects, manifestations of normal ageing may be mistaken for disease and lead to inappropriate prescribing. For example, drugs such as prochlorperazine are commonly misprescribed for giddiness due to age-related loss of postural stability. Not only is such treatment ineffective but the patient may experience serious side-effects such as drug-induced parkinsonism, postural hypotension, and mental confusion.

SELF-MEDICATION. Self-medication with over-the-counter products or with drugs prescribed for a previous illness (or even for another person) may be an added complication. Discussion with relatives and a home visit may be needed to establish exactly what is being taken.

SUSCEPTIBILITY. The ageing nervous system shows increased *susceptibility* to many commonly used drugs, such as opioid analgesics, benzodiazepines, and antiparkinsonian drugs, all of which must be used with caution.

PHARMACOKINETICS

While drug distribution and metabolism may be significantly altered, the most important effect of age is reduction in renal clearance, frequently aggravated by the effects of prostatism, nephrosclerosis, or chronic urinary tract infection. Many aged patients thus possess only *limited reserves of renal function, excrete drugs slowly,* and are *highly susceptible to nephrotoxic drugs*. Acute illness may lead to rapid reduction in renal clearance, especially if accompanied by dehydration. Hence, a patient stabilised on a drug with a narrow margin between the therapeutic and the toxic dose (e.g. digoxin) may rapidly develop adverse effects in the aftermath of a myocardial infarction or a respiratory tract infection.

ADVERSE REACTIONS

Adverse reactions often present in the elderly in a vague and non-specific fashion. *Mental confusion* is often the presenting symptom (caused by almost any of the commonly used drugs). Other common manifestations are *constipation* (with antimuscarinics and many tranquillisers) and postural *hypotension* and *falls* (with diuretics and many psychotropics).

HYPNOTICS. Many hypnotics with long half-lives have serious hangover effects of drowsiness, unsteady gait, and even slurred speech and confusion. Those with short half-lives should be used but they too can present problems (section 4.1.1). Short courses of hypnotics are occasionally useful for helping a patient through an acute illness or some other crisis but every effort must be made to avoid dependence.

DIURETICS. Diuretics are overprescribed in old age and should **not** be used on a long-term basis to treat simple gravitational oedema which will usually respond to increased movement, raising the legs, and support stockings. A few days of diuretic treatment may speed the clearing of the oedema but it should rarely need continued drug therapy.

NSAIDs. Bleeding associated with *aspirin* and *other NSAIDs* is more common in the elderly who are more likely to have a fatal or serious outcome. NSAIDs are also a special hazard in patients with cardiac disease or renal impairment which may again place the elderly at particular risk.

Owing to the *increased susceptibilty of the elderly* to the *side-effects of NSAIDs* the following recommendations are made:

- for *osteoarthritis, soft-tissue lesions and back pain* first try measures such as weight reduction, warmth, exercise and use of a walking stick;
- for *osteoarthritis, soft tissue lesions, back pain and rheumatoid arthritis* avoid giving an NSAID unless *paracetamol* (alone or with a *low dose* of an opioid analgesic as in co-codamol 8/500 or co-dydramol 10/500) has failed to relieve the pain adequately;
- where a paracetamol preparation has failed to relieve the pain adequately *add a very low dose of an NSAID* to the paracetamol preparation (starting with ibuprofen). For advice on prophylaxis of NSAID-induced peptic ulcers (where continued treatment with NSAIDs is necessary), see section 1.3.
- if an NSAID is considered necessary monitor the patient for gastro-intestinal bleeding for 4 weeks (and for a similar time on switching to another NSAID). For the management of NSAID-associated peptic ulcers, see section 1.3.
- do **not** give two NSAIDs at the same time.

Drug induced blood disorders are much more common in the elderly. Therefore drugs with a tendency to cause bone marrow depression (e.g. *co-trimoxazole, mianserin*) should be avoided unless there is no acceptable alternative.

The elderly generally require a lower maintenance dose of *warfarin* than younger adults; once again, the outcome of bleeding tends to be more serious.

GUIDELINES

First always question whether a drug is indicated at all.

LIMIT RANGE. It is a sensible policy to prescribe from a limited range of drugs and to be thoroughly familiar with their effects in the elderly.

REDUCE DOSE. Dosage should generally be substantially lower than for younger patients and it is common to start with about 50% of the adult dose. Some drugs (e.g. chlorpropamide) should be avoided altogether.

drugs and, ideally, these should not be given more than twice daily. In particular, regimens which call for a confusing array of dosage intervals should be avoided.

EXPLAIN CLEARLY. Write full instructions on every prescription (*including* repeat prescriptions) so that containers can be properly labelled with full directions. Avoid imprecisions like 'as directed'. Child-resistant containers may be unsuitable.

REPEATS AND DISPOSAL. Instruct patients what to do when drugs run out, and also how to dispose of any that are no longer necessary. Try to prescribe matching quantities.

If these guidelines are followed most elderly people will cope adequately with their own medicines. If not then it is essential to enrol the help of a third party, usually a relative or a friend.