Case 2—A 73-year-old man was treated from May 1977 with atenolol 100 mg daily and chlorthalidone for mild hypertension. In December he complained of symptoms of Raynaud's phenomenon in the hands. The dose of atenolol was reduced to 50 mg daily but four months later he complained of extremely painful feet and was found to have necrotic patches 0.5-2 cm diameter on the toes and sole of the right foot. Foot pulses were normal in both feet, and results of investigations were normal, as in case 1. The ischaemic lesions resolved completely within one month of discontinuing atenolol.

Case 3—A 48-year-old housewife was treated with bethanidine and cyclopentiazide-K for hypertension after her fifth pregnancy in 1972. In December 1976 propranolol 80 mg thrice daily was added because of poor control. Two weeks after starting propranolol she noticed pain in both feet and developed extensive areas of skin necrosis on the toes. Foot pulses were normal but loud epigastric and femoral bruits were heard. In view of her uncontrolled hypertension the dose of propranolol was increased to 160 mg thrice daily. Two months later the feet were more painful, with weeping of the areas of infarction. Femoral and renal angiography showed classical fibromuscular hyperplasia causing narrowing of both renal arteries and the left iliac arteries but no atheroma. Results of other investigations were normal. Propranolol was stopped and the necrotic patches cleared completely.

Comment

These patients present a distinctive picture of severe pain in the feet with multiple small areas of skin necrosis. All were non-smokers receiving recommended doses of beta-blockers, and none had a history of peripheral vascular disease. Symptoms worsened with increase in the dose of propranolol in one patient (case 3), and complete, rapid resolution occurred in each case after beta-blocker withdrawal. This picture differs from other reports of gangrene complicating beta-blockade^{3,4} in that foot pulses remained palpable in all cases. The onset of symptoms during the winter in each case supports a vascular aetiology affecting the small vessels. The mechanism of this complication is unknown; alpha-adrenergic agonist potentiation by beta-blocking agents may be responsible.⁵ Beta-blockers should be used with extreme caution in the presence of known peripheral vascular insufficiency.² The complaint of cold extremities during the winter in patients taking beta-blockers may precede serious tissue damage and is an indication for close observation or a change in treatment.

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Poisoning with tricyclic antidepressants: an avoidable cause of childhood deaths

Imipramine and amitriptyline are frequently prescribed for bed wetting in young children. These drugs are potentially lethal and are now the commonest cause of fatal poisoning in children under the age of 5 years.

Case report

A 4-year-old boy weighing 14 kg drank 90 ml of Tofranil Syrup (= 450 mg imipramine), which had been prescribed for his bed wetting. His mother, who was unaware of the poisonous nature of the drug, gave him a salt and water mixture, after which he vomited and then went to sleep. Four hours later he had a generalised fit, which lasted until he was given intravenous

diazepam in hospital. After this he remained unconscious but responded to painful stimuli. The electrocardiograph showed sinus rhythm with a rate of 180/min; his blood pressure was 110/70. Shortly after admission he developed ventricular tachycardia. Intravenous physostigmine and lignocaine failed to control this but after disopyramide, 25 mg given intravenously, sinus rhythm was restored. Cardiac monitoring was continued and he remained in sinus rhythm with a heart rate of 160-180 per minute until 18 hours after ingestion of the drug when he developed ventricular fibrillation. Sinus rhythm and an adequate circulation were restored by DC countershock but he had a further episode of ventricular fibrillation two hours later and could not be resuscitated.

Deaths due to accidental poisoning in children under 5 years of age

Years	No of patients		
	Salicylates	Iron preparations	Tricyclic antidepressants
1962-71	66	29	32
1972-6	6	6	17

Comment

Although accidental ingestion of drugs by young children is a common cause of hospital admissions, fatal poisoning is rare. In 1972 there were 16 000 such admissions and 25 deaths in the United Kingdom.¹ The numbers of deaths due to poisoning by preparations containing salicylates and iron have fallen dramatically in recent years and tricyclic antidepressants are now the commonest cause of fatal poisoning in children under the age of 5 years.²

Tricyclic antidepressants are the only drugs which are of any benefit in nocturnal enuresis and are widely prescribed for this purpose.³ Their exact mode of action is unknown but they affect both sleep patterns and the contractility of smooth muscle. They are seldom effective before the age of 7 or 8 years but are often prescribed, as in this case, for much younger children. Overdosage can cause convulsions, coma, cardiac arrhythmias, hypotension, and respiratory depression; there is no specific antidote, and treatment of massive overdosage is difficult. These effects have been well reported⁴ but there still seems to be widespread ignorance of the lethal nature of the drugs.

The age at which children acquire bladder control is very variable. Most are dry by day at the age of 5 years but roughly 10% of 5-year-olds wet the bed, as do 5% of 10-year-olds. While this is a great nuisance to the mother it seldom worries the child until he is 7 or 8 years old and its treatment with dangerous drugs cannot be justified. An explanation of the nature of enuresis to the child and his parents together with the use of a "star chart" will often produce dramatic improvement; if this fails a buzzer alarm, properly used, will cure at least 80% of enuretics in three months.⁵ We recommend, therefore, that no child with nocturnal enuresis should be treated with tricyclic antidepressants until he is at least 8 years old and has failed to respond to the above measures. The drugs should be dispensed only in tablet form in childproof containers which should carry a clearly visible warning about the lethal properties of their contents.

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