beats are often seen. These features may be due to enhanced automaticity; not surprisingly, as the heart rate slows and the myocardium becomes less ischaemic, automaticity decreases and the ventricular tachycardia disappears. Re-entry might, however, be the mechanism responsible; fractionation of ventricular depolarisation is increased by cardiac acceleration and thus re-entry ventricular arrhythmias might be produced. When the heart is vulnerable—for example, because of critical coronary artery disease—ventricular fibrillation may be precipitated, but under the conditions of exercise testing immediate resuscitation is at hand.[15 17]

Coronary artery bypass surgery is clearly indicated in the presence of severe angina and ventricular arrhythmias and may be justified for persistent ventricular arrhythmias even if beta-blocking treatment seems to control angina. Case 12 fell into this category although adequate venous grafting was found to be impossible. Antiarrhythmic therapy with quinidine, mexiletine, amiodarone, and disopyramide alone and in combination was unsuccessful in this patient but should be tried first in such circumstances.

There is some evidence that in particular distributions of coronary artery disease death can be prevented by coronary artery bypass surgery—for example, left main stem disease.[18] If part of this beneficial effect is due to the prevention of life-threatening ventricular arrhythmias it is imperative to detect clinical features suggesting such arrhythmias. Although ventricular arrhythmias, and particularly the more severe forms, are less reproducible on ambulatory monitoring than on exercise testing,[2] they are more common on the former,[19] and ambulatory monitoring and stress testing are complementary.[2 10] They disclose ventricular arrhythmias at different times and both must be used to identify such patients at risk.

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References

1 Goldschlager, N, Cake, D, and Cohn, K, *American Journal of Cardiology*, 1973, **31**, 434.
2 Ryan, M, Lown, B, and Korn, H, *New England Journal of Medicine*, 1975, **292**, 224.
3 Raftery, E B, and Cashman, P M, *Postgraduate Medical Journal*, 1976, **52**, suppl No 7, p 32.
4 Chiang, B N, *et al*, *Annals of Internal Medicine*, 1969, **70**, 1159.
5 Bruce, R A, *et al*, *American Heart Journal*, 1973, **85**, 546.
6 Judkins, M, *Radiology*, 1967, **89**, 815.
7 Jelinek, M V, and Lown, B, *Progress in Cardiovascular Disease*, 1974, **16**, 496.
8 Vedin, J A, *et al*, *American Journal of Cardiology*, 1972, **30**, 25.
9 McHenry, P L, *et al*, *American Journal of Cardiology*, 1976, **37**, 609.
10 Nixon, J V, *et al*, *Circulation*, 1978, **57**, 115.
11 Tilkian, A G, *et al*, *American Heart Journal*, 1976, **92**, 707.
12 Nakhjavan, F K, *et al*, *Journal of the American Medical Association*, 1971, **216**, 2138.
13 Ecker, R R, *et al*, *Circulation*, 1971, **44**, 666.
14 Cline, R E, Armstrong, R G, and Stanford, W, *Journal of Thoracic and Cardiovascular Surgery*, 1973, **65**, 802.
15 Irving, J B, and Bruce, R A, *American Journal of Cardiology*, 1977, **39**, 849.
16 Gallagher, J J, *et al*, *American Journal of Cardiology*, 1975, **35**, 696.
17 McHenry, P L, *American Journal of Cardiology*, 1977, **39**, 935.
18 Takaro, T, *et al*, *Circulation*, 1976, **54**, suppl No 3, p 111.
19 Vismara, L A, *et al*, *American Journal of Cardiology*, 1977, **39**, 821.

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SIDE EFFECTS OF DRUGS

Diflunisal-induced cholestatic jaundice

Diflunisal (Dolobid) is a recently introduced analgesic chemically related to aspirin. It has fewer side effects than aspirin but caused a mild increase in the serum concentration of aspartate transaminase (serum AST; SGOT) in one patient.[1] Jaundice, however, has not been recorded. I report a case of cholestatic jaundice due to diflunisal.

Case report

A 64-year-old school caretaker had complained of lumbar pain radiating to his right thigh for over a year. Radiography confirmed arthritic changes in the lumbar spine. In February 1978 his symptoms kept him away from work and he was given fenoprofen (Fenopron) 600 mg three times a day. This was supplemented with dextropropoxyphene and paracetamol (Distalgesic) and his symptoms improved. He resumed work after three weeks' absence. In March his symptoms recurred but on this occasion were not improved by fenoprofen and Distalgesic. Indomethacin (Indocid) 25 mg three times a day was therefore substituted for fenoprofen. The dosage of indomethacin was doubled after two weeks in an effort to control his symptoms. After four days on the higher dosage of indomethacin the Distalgesic was stopped and diflunisal started, the indomethacin being reduced to 25 mg three times a day.

The diflunisal was given in an initial dose of two tablets (500 mg) followed by one tablet twice a day, as recommended by the manufacturers. After five days the patient complained of mild pruritus, pale stools, and dark urine. His pain had been well controlled. On examination he was found to be clinically jaundiced and apyrexial. There was no lymphadenopathy; chest and heart were normal; the abdomen was soft with no enlargement of gall bladder, liver, or spleen; rectal examination disclosed only pale stools; and urine contained bilirubin. Cholestatic jaundice was diagnosed and diflunisal stopped. He continued to take the indomethacin.

Results of laboratory investigations on the day the diflunisal was stopped were: haemoglobin 15·4 g/dl; white cell count 6×10^9/l (6000/mm^3), normal differential; erythrocyte sedimentation rate (ESR) 10 mm in first hour; serum urea and electrolytes normal; total bilirubin 57 μmol/l (3·3 mg/100 ml); alkaline phosphatase 780 IU/l (normal 120-300 IU/l); and serum AST 120 IU/l (normal less than 40 IU/l). Urine contained a normal amount of urobilinogen; bile salts and bilirubin were detected; a midstream specimen was sterile and contained no excess of cells; and hepatitis B antigen was not detected in the serum. Three days later the serum bilirubin was 71 μmol/l (4·2 mg/100 ml), alkaline phosphatase 800 IU/l, and AST 105 IU/l. Four days later the bilirubin was 55 μmol/l (3·2 mg/100 ml), and 12 days after the diflunisal was stopped an oral cholecystogram showed a normal functioning gall bladder with no evidence of calculi. A chest radiograph was normal. Neither antimitochondrial antibodies nor smooth-muscle antibodies were detected.

Thirty days after the diflunisal was stopped the serum bilirubin was less than 17 μmol/l (1·0 mg/100 ml), alkaline phosphatase 750 IU/l, and AST 50 IU/l. Physical examination showed no enlargement of liver, gall bladder, or spleen, and no other abnormality could be detected. Eighteen days later the haemoglobin was 14·8 g/dl, ESR 5 mm in first hour, total bilirubin less than 17 μmol/l, alkaline phosphatase 450 IU/l, and serum AST 30 IU/l. Sixty-eight days after stopping diflunisal the serum alkaline phosphatase was 275 IU/l and AST 20 IU/l. Thus the drug-induced hepatitis had resolved.

Comment

While this patient was taking diflunisal and indomethacin he developed cholestatic jaundice, and when the diflunisal was stopped and the indomethacin continued the jaundice gradually cleared. He is still taking indomethacin and Distalgesic.

Indomethacin has been implicated in hepatitis.[2] Diflunisal may increase plasma concentrations of indomethacin by up to 35%.[3] In this case, before the introduction of diflunisal the patient was taking 150 mg of indomethacin daily and when the diflunisal was introduced the dose of indomethacin was halved. Thus it seems highly unlikely that the indomethacin caused the jaundice. It must be concluded that diflunisal was the cause; the time interval from the beginning of the

treatment to the appearance of the jaundice conforms with other cases of drug-induced jaundice.

[1] Kaklamanis, Ph, *et al*, *Journal of Clinical Therapeutics*, 1978, **1**, suppl A, p 4677.
[2] Kelsey, W M, and Scharyj, M, *Journal of the American Medical Association*, 1967, **199**, 586.
[3] Tempero, K F, Crillo, V G, and Steelman, S L, *British Journal of Clinical Pharmacology*, 1977, **4**, suppl 1, p 31.

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Contact allergy to clotrimazole

Clotrimazole (Canesten; diphenyl-2-chlorophenyl-1-imidazolylmethane) is an effective broad-spectrum antifungal agent that has been used in Great Britain since 1973. In clinical trials only a few patients have been irritated by clotrimazole and no cases of contact allergy have been reported. I describe a patient who developed contact allergic dermatitis to clotrimazole.

Case history

A 48-year-old policeman had had perineal and perianal pruritus for many years. In September 1977 he was prescribed Canesten cream, which he used intermittently for the next few months. In December, after applying Canesten cream, he noticed an increase in the pruritus accompanied by an erythematous, oozing rash over his scrotum, upper thighs, and natal cleft. He discontinued the Canesten, and Tri-Adcortyl cream was prescribed. His rash gradually improved.

Patch tests were applied for 48 hours using the Finn Chamber method and inspected at 48 and 96 hours. At both times reactions were seen to Canesten cream, 1% clotrimazole in ethyl methyl ketone, and 1% ethylene diamine in yellow soft paraffin. Results were negative with Canesten cream base and Tri-Adcortyl cream.

Comment

Canesten cream consists of the active ingredient clotrimazole and the base, which contains Arlacel 60, Tween 60, spermaceti, Lanette 0, Eutanol G, benzyl alcohol, and demineralised water. During clinical trials of clotrimazole 1% cream Weuta[1] found irritation in 5% of patients. In clinical evaluations of clotrimazole, Spiekermann and Young[2] recorded adverse effects in 2·7% of patients, and Clayton and Connor[3] reported that 15% of patients using clotrimazole cream experienced transient burning and irritation. No cases of allergic contact dermatitis were reported. Wahlberg[4] obtained negative patch test results in patients with eczema using clotrimazole cream in concentrations 16 and 32 times greater than normal.

Only one case of patch-test-proved contact allergy has been reported (J Ward-Jenkins, Bayer UK Limited, personal communication). The present patient had patch-test-proved contact allergic dermatitis to clotrimazole. As this effective antifungal agent achieves more widespread use, more patients will be likely to develop allergy to clotrimazole.

[1] Weuta, H, *Drugs Made in Germany*, 1972, **15**, 126.
[2] Spiekermann, P H, and Young, M D, *Archives of Dermatology*, 1976, **112**, 350.
[3] Clayton, Y M, and Connor, B L, *British Journal of Dermatology*, 1973, **89**, 297.
[4] Wahlberg, J E, *Münchener medizinische Wochenschrift*, 1976, **118**, 76.

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(*We suggest to readers that any suspected adverse reaction to a new drug should be reported to the Committee on Safety of Medicines, preferably on a yellow card. Serious or unusual reactions to all drugs should also be reported.*)

SHORT REPORTS

Ingrowing toenails in infancy

Ingrowing of the great toenail is common in older children and adults, and is generally attributed to convex cutting of the nail.[1] A more complex theory has been put forward suggesting that there is an imbalance between the nail and cuticle borders due to incurving of the medial side of the toe, influenced by inherited architecture and compounded by pointed-toe and high-heeled shoes. Careless cutting back of the corners of the nail then initiates chronic inflammation.[2] The condition has not been described in infants, and we report two cases.

Case reports

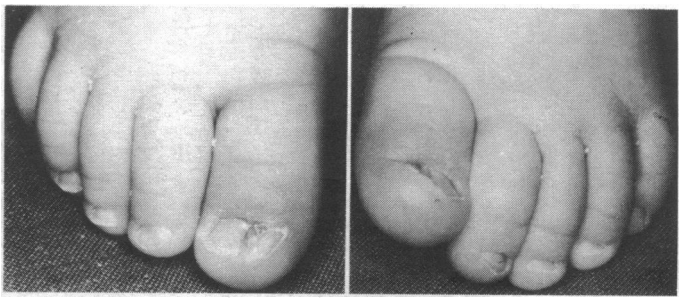
Case 1—A 10-week-old boy presented with bilateral acute paronychia of the great toenails of two weeks' duration (figure). There was no reason to believe that he had been wearing tight clothes or shoes; his toenails had never been cut; and he did not suck his toes. There was a family history of ingrowing toenails: the patient's paternal grandmother had required removal of both great toenails at the age of 2 years, and a maternal cousin had required antibiotic treatment for redness of the great toes at the age of 4 months, suggesting ingrowth of the nails. The boy was treated by avulsion of both great toenails under general anaesthesia; the infection settled completely, but the nails grew inwards again within two months. Tin foil placed beneath the toenail margin was unsuccessful in stopping this, and the problem is as yet unresolved.

Case 2—A 6-week-old boy developed ingrowing of the right great toenail with surrounding inflammation, but no pus was produced. There was no family history. From birth he had been put down to sleep prone, and the changes in the toenail had occurred at the time when he had started kicking very actively. The condition was attributed to constant rubbing, and settled rapidly when he started to sleep on his back. Nevertheless, it recurred at the age of 2½ years after he had been wearing narrow shoes; it responded to a course of co-trimoxazole.

Comment

In their analysis of ingrowing toenails in different age groups, Murray and Bedi[3] did not mention infants. The only suggestion of an inherited disorder in published reports, other than Lathrop's theory,[2] is by Chapman,[4] who describes a condition of overcurvature of the toenails as a result of which the nail cuts into the lateral nailfold; this occurs, however, in young adult life. Paronychia of the thumb may occur in infants as a result of sucking.[5]

The family history in case 1, and the recurrent nature of the condition in both cases, suggest that there may be an inherited tendency for the great toenails to grow inwards, perhaps requiring an additional



Case 1. Bilateral acute paronychia of great toenails.