in vertex presentation (rate ratio was 1·1 for spontaneous, low forceps, and mid-forceps deliveries, but 0·9 for caesarean sections and 0·8 for breech deliveries).

Comment

It is recognised that demonstrable trauma associated with difficult operative vaginal delivery, resulting in bruising, leads to neonatal jaundice. When such clinically apparent cases were excluded by Campbell *et al*,[5] however, they still found more instrumental procedures in the jaundiced group. We would suggest that operative instrumental delivery may cause focal haemorrhages that are not readily detectable in the infant, but may nevertheless subsequently be manifested by the appearance of jaundice.

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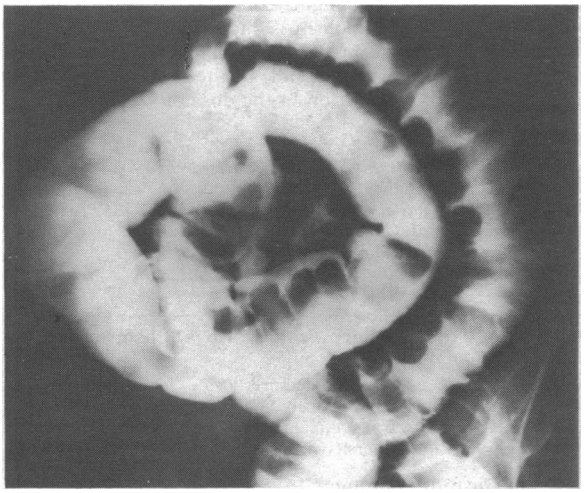
Successful treatment of pneumatosis coli with oxygen

Pneumatosis coli is a condition of multiple gas-filled cysts in the subserosal and submucosal layers of the large bowel. Forgacs *et al*[1] first described successful treatment with high concentrations of oxygen. Since then there have been only a few similar reports.

Case report

A 69-year-old woman presented with a 12-month history of excessive flatus and a 6-month history of passing up to 10 small motions daily. She had suffered from chronic obstructive airways disease for more than 40 years. She had never smoked and the plasma α-1-antitrypsin was normal at 2·4 g/l (0·024 mg/100 ml). She also had mild angina of effort and had had three minor cerebral thromboses with residual right-sided weakness and nominal dysphasia. She had taken corticosteroids for five years for her chest disease and had developed diabetes mellitus, which was controlled by diet and glibenclamide.

She had a distended, tympanic abdomen. A polypoid mobile mass was palpable in the rectum. Sigmoidoscopy, abdominal *x*-ray examination, barium enema, colonoscopy, and rectal biopsy showed features of pneumatosis coli (fig 1). She was treated with high concentration oxygen for 20 hours daily for five days. An arterial oxygen tension of 40·5 kPa (304 mm Hg) was easily achieved with a 60% oxygen face mask and nasal cannulae at 4 l/min. The response to treatment was dramatic. Within 48 hours the frequent bowel movements ceased and the bowel habit was still normal after five months. The rectal mass disappeared rapidly and a repeat colonoscopy (one week) and barium enema (one month) showed a normal colon.



Barium enema before treatment showing multiple cystic filling defects.

Discussion

The patient's symptoms and the presence of a rectal mass suggested a diagnosis of rectal carcinoma but the simple investigations of plain abdominal *x*-ray examination and sigmoidoscopy were diagnostic of pneumatosis coli, and major surgery in a high-risk patient was avoided. The case exemplifies the association between pneumatosis of the bowel and obstructive airways disease,[2] and this should be remembered when patients with lung disease present with diarrhoea or a change in bowel habit. Rectal bleeding and prolapse may also occur.[3 4]

High concentration oxygen treatment is a cheap and simple form of treatment for pneumatosis coli. Although the cause of the condition is unknown, Forgacs *et al*[1] correctly predicted that displacing nitrogen with oxygen in the lungs, and thus reducing the total partial pressures of gases in the venous blood, would deflate the cysts. They emphasised that oxygen administration must be continuous, but Dean and Castleden[5] found intermittent therapy effective and allowed the patient more freedom.

I thank Dr Lindsay Davidson for his helpful criticism and permission to report this case.

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Ocular toxicity due to rifampicin

Rifampicin is widely used as one of the first-line drugs in the chemotherapy of tuberculosis. Though oculotoxic effects such as loss of acuity of vision and colour blindness have been reported in a case treated with both rifampicin and ethambutol,[1] rifampicin alone has not yet been reported to be oculotoxic. We report below a case of reversible rifampicin oculotoxicity.

Case report

A 34-year-old man suffering from pulmonary tuberculosis (AFB-positive) was given daily the triple oral regimen of isoniazid (300 mg), rifampicin (450 mg), and ethambutol (1200 mg). After a week both eyes were painful, tender, red, and congested with thick white secretions. The drugs were stopped and the eyes cleared up within 72 hours. Treatment was then changed to isoniazid, PAS (10 g daily), and streptomycin (0·75 g intramuscularly daily for five days a week). He developed nausea and vomiting, probably due to PAS, and the drugs were stopped. He was then kept on isoniazid (300 mg daily) only for a week. There were no adverse reactions. Rifampicin (450 mg daily) was then added, and within 48 hours the same type of ocular reactions again developed. He was not taking any other drug

known to be oculotoxic, and the eyes cleared up within 48 hours after stopping rifampicin. He was put on isoniazid, ethambutol, and streptomycin without any untoward reactions and he became AFB-negative. He was later discharged on oral isoniazid and ethambutol.

Signs of toxicity in a patient taking various combinations of antituberculosis drugs

Drug regimen	Ocular toxicity	Liver function tests	Other toxicity
None	–	Normal	–
Isoniazid, ethambutol, and rifampicin	+	Normal	–
Isoniazid, PAS, and streptomycin	–	Normal	Vomiting, nausea
Isoniazid (one week)	–	Normal	–
Isoniazid and rifampicin	+	Normal	–
Isoniazid, ethambutol, and streptomycin	–	Normal	–

Comment

Clearly the exudative conjunctivitis in this case might have been due to rifampicin—perhaps a kind of hypersensitivity or idiosyncratic reaction.

[1] *Extra Pharmacopoeia: Martindale*, ed N W Blacow and A Wade, 26th edn, p 1416. London, Pharmaceutical Press, 1972.

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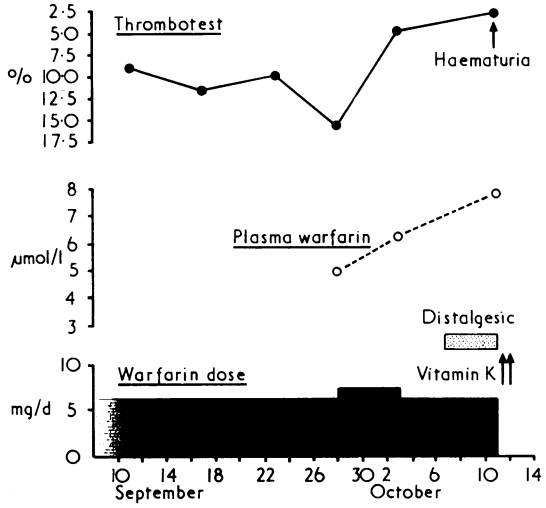
Warfarin and Distalgesic interaction

Many patients receiving long-term anticoagulant treatment with warfarin require an analgesic from time to time. Current practice suggests that they should not be given acetylsalicylic acid because of an increasing risk of haemorrhage. It is common clinical practice, therefore, to recommend either paracetamol or Distalgesic for pain relief in these patients. We report two patients on warfarin who had definite haematuria when given Distalgesic (dextropropoxyphene hydrochloride and parautamol.)

Case reports

Case 1—A 55-year-old man presented in July 1972 with a deep vein thrombosis of his left leg, which was confirmed by venography. He was well controlled initially on 6 mg of warfarin daily but on 28 September his thrombotest was 16% and his dose of warfarin was increased to 7 mg/day (the plasma warfarin concentration at this stage was 4·9 μmol/l (1·5 μg/ml)). On 3 October the dose of warfarin was reduced back to 6 mg per day because the thrombotest was only 5% (the plasma warfarin concentration was now 5·9 μmol/l (1·8 μg/ml)). On 11 October he presented with marked haematuria and his thrombotest was less than 5%. He had had an episode of back pain on 6 October for which he had taken Distalgesic, two tablets three times daily. The plasma warfarin concentration on admission was 7·8 μmol/l (2·4 μg/ml), having risen from 5·9 μmol/l (1·8 μg/ml) in spite of the reduction in the dose of warfarin. He was given vitamin K and his haematuria disappeared over the next three days.

Case 2—A 75-year-old woman was first seen in November 1974, when she presented with dyspnoea and pleuritic chest pain and a diagnosis of pulmonary embolism was made. She was treated with heparin and then maintained on warfarin and, on a steady dose of 7 mg/day, the prothrombin time varied between 30 and 40 seconds (optimal anticoagulant control 28-36 seconds). On 6 January 1975, after six weeks' treatment with warfarin she was prescribed Distalgesic for a pain in her leg. She took six tablets between 1200 and 1800 hours and presented in casualty at 2300 hours with gross haematuria. Her prothrombin time was 130 seconds and, after being given 10 mg vitamin K, the haematuria resolved over the succeeding four days. No measurements of plasma warfarin concentration were made.



Thrombotest percentages, plasma warfarin concentrations, and warfarin daily dosages in case 1. Plasma warfarin concentrations were measured by the method of Lewis *et al.*[5]

Conversion: SI to traditional units—Warfarin: 1 μmol/l ≈ 0·31 μg/ml.

FURTHER STUDIES

To examine the possible mechanism whereby Distalgesic might potentiate the effect of warfarin, studies were done with dextropropoxyphene in both man and rats. Paracetamol has been shown not to interfere significantly with the hypoprothrombinaemic effect of warfarin, in the usual clinical doses of up to 3·0 g per day.[1 2] Dextropropoxyphene in concentrations of 3·0 μmol/l (1·0 μg/ml), 14·7 μmol/l (5·0 μg/ml), and 29·5 μmol/l (10·0 μg/ml) did not displace warfarin (16·3 μmol/l (5·0 μg/ml)) from protein-binding sites in human plasma in studies using an ultrafiltration technique.[3]

Groups of rats were treated with dextropropoxyphene in a dose of 20 mg/kg, and the sleeping times and plasma half-lives of ^{14}C-pentobarbitone were recorded.[4] The mean pentobarbitone sleeping time in a group of 10 rats treated with dextropropoxyphene was 156·4 ± 9·1 (SEM) minutes while that of the control rats given saline was 106·8 ± 5·9 minutes ($P<0.005$). The half-life of ^{14}C-pentobarbitone (30 mg/kg) was 202·0 ± 27·8 (± 95% confidence limits) minutes in the animals treated with dextropropoxyphene, compared with 101·0 ± 9·5 minutes in the control animals.

Discussion

In both patients Distalgesic apparently potentiated the hypoprothrombinaemic effect of warfarin, with resultant haematuria. Our studies suggest that dextropropoxyphene does not displace warfarin from plasma-protein-binding sites. Animal studies suggest that dextropropoxyphene inhibits the metabolism of pentobarbitone, as judged by pentobarbitone sleeping time and half-lives. Dextropropoxyphene is metabolised by the same liver microsomal enzymes that hydroxylate warfarin and might compete for metabolism. This inhibition of warfarin metabolism is supported by the measurement of plasma warfarin concentrations, which rose from 5·9 μmol/l (1·8 μg/ml) to 7·8 μmol/l (2·4 μg/ml) in the first patient when given distalgesic in spite of a reduction in the dose of warfarin.

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