adverse reactions to a particular drug. Both the Swedish and UK regulatory agencies issued warnings, but their substance and emphasis differed, and this may have introduced some bias; neither regulatory authority, though, emphasised the problem of peripheral neuropathy, which appears to be the major difference in the profiles of adverse reactions to the drug.

We are grateful to Dr B E Wiholm of the National Board of Health and Welfare, Department of Drugs, Sweden, and Dr B H Ch Stricker of the Netherlands Centre for the Monitoring of Adverse Reactions to Drugs for their help and for supplying national data. We are also

grateful to the Committee on Safety of Medicines for permission to quote from the UK Adverse Reactions Register, and to Professor Abe Goldberg for his invaluable help and criticism.

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SHORT REPORTS

Unusual complication of perforated appendix

Peritonitis, local or generalised, is a common accompaniment of acute appendicitis, and residual septic foci may occur. The incidence of these has decreased over recent years, partly as a result of improved surgical techniques but largely owing to the use of prophylactic antimicrobial agents,¹ whether local^{2 3} or systemic.⁴

We routinely use antibiotic peritoneal lavage (using a solution of 1 g tetracycline/1 0.9% saline) in cases of peritoneal sepsis, with good results.^{2 3} Residual intraperitoneal sepsis may still occasionally occur in the form of pelvic, interloop, and subphrenic abscesses, in addition to local sepsis in relation to the appendix stump. We describe an abscess in the scrotum after appendicectomy.

Case report

A 9-year-old boy was admitted with a two-day history of colicky central abdominal pain that localised in the right iliac fossa on the day of admission. He was toxic, and examination suggested acute appendicitis with peritonitis. At laparotomy, through a grid-iron incision, a perforated retrocaecal appendix was found with free pus in the peritoneal cavity. Culture of the pus subsequently yielded a profuse growth of *Escherichia coli*. After appendicectomy thorough peritoneal lavage with tetracycline in saline was carried out, and the wound was closed without drainage. No other antibiotic was given.

After the operation he had a slight fever, which was attributed to a low-grade wound infection. The sutures were removed on the sixth postoperative day, and on the same day he developed quite suddenly a painful, hot, red swelling of the right side of his scrotum. Torsion of the right testis was provisionally diagnosed and exploration carried out. On opening the tunica vaginalis 5 ml of pus was released, but the testis and epididymis were normal. The wound was drained. His fever settled rapidly and he made an uneventful recovery. Culture of the pus proved sterile. Subsequent outpatient review at three months showed no evidence of further sepsis.

Comment

Co-existence of a perforated appendix and right-sided congenital hydrocoele or hernia must be common, yet we could find no report of residual sepsis in the scrotum. Our patient had no history or clinical finding suggestive of a hydrocoele or hernia, but presumably a connection between the peritoneal cavity and the tunica vaginalis was present. A patent processus vaginalis was not found at the second operation, but obliteration of the channel after the sepsis is probable. Spread of the sepsis from the abdominal wound into the inguinal canal seems unlikely, as the sepsis in the scrotum was confined within the tunica vaginalis.

Acute epididymo-orchitis after prostatic surgery is well recognised, infection reaching the testis via the vas deferens. It might be postulated that retroperitoneal infection from a retrocaecal appendix could track alongside the vas, but in this case there was no evidence of infection of the epididymis or testicle.

Opponents of intraoperative peritoneal lavage believe that it may spread sepsis within the peritoneal cavity. We have been unable to find any evidence for this view, but it is conceivable that the lavage encouraged the passage of organisms down a patent processus. It is unlikely that the use of systemic antibiotics would have prevented this

occurrence. Recent (unpublished) observations have shown that tetracycline lavage leads to a therapeutic serum tetracycline concentration within an hour, and the pus trapped in the scrotum was shown to be sterile. It is therefore difficult to know how this complication might be avoided, even when a congenital hernia or hydrocoele is suspected before operation.

We thank Mr S S Miller, consultant surgeon at the Royal Aberdeen Children's Hospital, for permission to report on his patient.

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Hypophosphataemic vitamin-D resistant rickets may need phosphate supplements

The commonest form of vitamin-D resistant rickets is associated with a renal tubular defect producing hyperphosphaturia and hypophosphataemia, and has been treated with vitamin D up to 100 000 units daily together with phosphate supplements.¹ Recent reports^{2 3} suggest that phosphate supplements are not required when treatment is with 1 α -hydroxy vitamin D₃ (1 α -OHD₃), but the results show that serum phosphate concentrations remained subnormal. We describe a child in whom rickets was not controlled with 1 α -hydroxy vitamin D₃ until oral phosphate supplements were given.

Case report

A girl delivered at full term after breech presentation weighed 3150 g and was bottle fed. Welfare clinic multivitamin drops were given daily for one year. Her parents, brother, and sister were healthy and there was no family history of bone disease. She was very active, had a good appetite, and the milestones of development were normal. She walked at 13 months but her gait was waddling and her legs became increasingly bowed. When she presented at 23 months her height was -3 SD and weight -2 SD from the mean (76 cm and 9.6 kg). Radiographs showed evidence of severe rickets affecting wrists and knees. Results of investigations were: serum calcium concentration 2.5 mmol/l (10.1 mg/100 ml); phosphate concentration 0.7 mmol/l (2.1 mg/100 ml); alkaline phosphatase activity grossly raised;

parathyroid hormone concentration 0.6 ng/ml (normal <1.0); and 25-hydroxycholecalciferol concentration 46 nmol/l (18.5 ng/ml) (normal 10-75 nmol/l; 4-30 ng/ml). Blood gases, amino-acids, urea and electrolyte concentrations, and results of ophthalmic slit-lamp examination were normal. Urine pH was 5.0; calcium concentration was under 1 mmol/l (4 mg/100 ml) and phosphate concentration 13.4 mmol/l (41 mg/100 ml).

The patient was treated with vitamin D and oral phosphate, which were serially adjusted to heal the rickets and prevent hypercalcaemia and hypophosphataemia (figure). When she was aged 5 years 1 α -hydroxy vitamin D₃

Serial calcium and phosphate concentrations and alkaline phosphatase activity related to treatment from 23 months of age onwards.

Conversion: SI to traditional units—Calcium: 1 mmol/l $\approx$ 4.0 mg/100 ml. Phosphate 1 mmol/l $\approx$ 3.0 mg/100 ml.

was substituted for vitamin D and simultaneously phosphate supplements were stopped. Serum phosphate concentrations promptly fell, and alkaline phosphatase activity rose. After 11 months radiography of the wrists showed no abnormality, but the knees showed florid rickets. Phosphate supplements were restarted, reversing the hypophosphataemia and hyperphosphatasia, and the rickets healed. The doses of 1 α -hydroxy vitamin D₃ and phosphate were serially adjusted to maintain normal serum concentrations of calcium and phosphate. She was overactive with difficult behaviour during the hypophosphataemic period. Her height gradually increased from the first to the tenth centiles over the five years of treatment. The initial bowing of the femora cleared and she lived an otherwise normal schoolgirl life.

The child continued with the same dose of 1 α -hydroxy vitamin D₃ as when rickets was present, yet she was normal with the help of phosphate supplements.

Comment

Vitamin D increases the absorption of dietary calcium and phosphate but does not prevent the excessive renal loss of phosphate that is characteristic of hypophosphataemic vitamin-D resistant rickets.¹ Recent reports suggest that the condition is well controlled using 1 α -hydroxy vitamin D₃ in high pharmacological doses of 0.5-2.0 μ g/kg body weight daily.^{2,3} Our patient developed hypercalcaemia with only 0.1-0.15 μ g/kg body weight daily and the danger of hypercalcaemia increases with higher doses. The highest recorded serum phosphate concentration in children treated with 1 α -hydroxy vitamin D₃ alone was 0.97 mmol/l (3.0 mg/100 ml), the normal childhood range being 1.3-1.9 mmol/l (4.0-6.0 mg/100 ml).² In similarly treated adults the mean serum phosphate concentration was only 0.76 mmol/l (2.3 mg/100 ml), the normal adult range being 0.8-1.3 mmol/l (2.4-4.0 mg/100 ml).³ Our patient developed normal concentrations only when phosphate supplements were given. Her abnormal overactive behaviour during the hypophosphataemic phase accords with the known whole-body effects of hypophosphataemia.⁴

Population surveys for rickets depend radiologically on pictures of wrists but our experience with this child shows the importance of also including the knees.⁵ We suggest that the logical method of treating this condition is with low doses of 1 α -hydroxy vitamin D₃ to-

gether with phosphate supplements. The likelihood exists that phosphate will prove equally necessary in the treatment of other forms of renal hypophosphataemic rickets.

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Role of tartrazine in chronic urticaria

Reactions to azo dyes, particularly the yellow dye tartrazine, are often reported. The proportion of patients with chronic urticaria who develop an exacerbation after taking tartrazine has ranged from 5 to 36%.^{1,2} Salicylates, usually in the form of aspirin, will cause similar exacerbations, affecting 20-45% of patients with chronic urticaria.³ Many patients who have a reaction to salicylate in an active phase of chronic urticaria can take salicylates again when the urticaria is clear.

When patients with chronic urticaria are challenged with a battery of substances, including salicylates and tartrazine, those who react to one are frequently affected by the other.⁴ We tested 317 patients: 40 (13%) reacted to tartrazine and 28 of these also reacted to salicylates. The mechanisms of tartrazine and salicylate reactions in chronic urticaria are probably similar and non-immunological. This view would be strengthened if it was shown that patients who had previously developed exacerbations of urticaria owing to tartrazine no longer reacted once their urticaria was clear.

Patients, methods, and results

From 40 patients with chronic urticaria who had previously reacted to 10 mg tartrazine we selected 20 who lived near Bristol. Thirteen agreed to come to hospital for further tests but one defaulted, so that the tests were carried out in 12 patients (seven women, five men; average age 44 years, range 17-71). Each patient was given three identical capsules—lactose, tartrazine 10 mg, and lactose—which were taken on alternate mornings. One to four weeks later a test dose of 1 mg tartrazine was given interspersed with two other colours as part of a different investigation.

The development of widespread weals between two and eight hours after the capsule was taken was recorded as a positive reaction. Five patients who had been clear of urticaria for one-and-a-half to seven years had no reaction to 10 mg and 1 mg tartrazine; two who had been clear for two to three years except for minor episodic attacks had no reaction to 10 mg and 1 mg tartrazine; and three who had been clear for three to eight weeks showed a reaction to 10 mg tartrazine but none to 1 mg tartrazine. Two patients still with active urticaria (present for three and seven years) showed reactions to both 10 mg and 1 mg tartrazine.

Comment

In the 12 patients tested reactions to tartrazine occurred when the urticaria was in an active phase or shortly afterwards, and did not occur when the urticaria had been clear for a long period. The effect is quantitative since the two patients reacting to 1 mg tartrazine were the only ones with active urticaria. In another series of 56 patients with chronic urticaria⁵ immediate and 48-hour patch tests were carried out to 2% tartrazine. These were all negative, including in four patients who had reacted to oral challenge tests of 10 mg tartrazine.