abdominal pain, virtual obstruction of the rectum, and dyspareunia due to two recurrent pelvic hydatid cysts. She had been treated with mebendazole 50 mg/kg for one year without benefit.

All patients were monitored for bone marrow, hepatic, or renal toxicity. Two patients became feverish within 48 hours of beginning treatment; the only other symptoms complained of were pain in the area of the cyst in one patient and headache and nausea in another.

One of our patients failed to respond to two months' albendazole treatment. She developed an anaphylactic reaction two weeks after stopping the drug and was admitted to another hospital, where laparotomy failed to detect obvious rupture of the cyst and it was removed.

In the remaining three patients there was evidence of improvement. A repeat CT scan in case 1 showed a dramatic reduction in size of all cysts after one month's treatment. In the second patient an ultrasound scan showed pronounced reduction in the size of the cyst, and regular drainage of 100 ml/day from an intercostal chest drain became minimal during the first week of treatment. In the remaining case the tension of the cysts (easily assessable on rectal examination) was noticeably reduced at one month; the drug was continued for a second month, after which there was pronounced symptomatic improvement. Repeat CT scan showed reduction in cyst size and loss of the spherical shape of the cysts. On rectal examination the cysts were found to be soft, rather like a half-filled hot-water bottle.

Three of the four patients had a positive complement fixation test result (1/32) before treatment; and two showed a two-titre improvement in hydatid complement fixation tests after treatment. In the remaining patient, who failed to improve, there was initially an encouraging fall in the complement fixation test result, but this returned to the pretreatment value at the end of two months' treatment.

The blood concentrations of albendazole sulphoxide (a metabolite with anthelmintic activity) were measured by high-performance liquid chromatography.⁵ The parent drug albendazole was not detected. The mean of peak albendazole sulphoxide concentrations was just below 1000 µg/l (table). The

Blood concentrations of albendazole sulphoxide in the four patients

Case No	Dose	Administration times (hours)	Day of treatment	Sample time (hours)	Albendazole sulphoxide (µg/l)
1	400 mg twice daily	0 + 7	8	1	1830
				4	1820
				7	1330
2	400 mg twice daily	0 + 7	5	5	670
				1	50
				2	160
3	400 mg twice daily	0 + 7	5	4	340
				8	880
				12	280
				21	20
				24	20
				4	460
4	400 mg morning, 200 mg evening	0 + 7	5	1	170
				2	430
				4	260
				8	460
				12	140
				21	30
				24	90
				4	420

two serial studies suggest that albendazole sulphoxide is rapidly eliminated from plasma, and serum concentrations after one week's treatment were little different from those attained during the first 24 hours.

Comment

Albendazole produced radiographic evidence of cyst regression in three of our first four patients treated with this drug. In one patient continuous external drainage of cyst fluid stopped on beginning treatment. Subsequent observation at three to six months showed no evidence of recurrence but it was too early to assess long-term results.

The serological improvement in treated cases was also encouraging. The serum concentrations of albendazole sulphoxide achieved at 10 mg/kg were some one hundred times better than would be expected with the same dose of mebendazole.

The speed of shrinkage of cysts in a solid structure such as the liver may well be slower than for cysts in other sites. The duration of treatment in the former may need further consideration. The concentrations of albendazole achieved in these cysts is as yet unknown.

Albendazole has been shown to be teratogenic and embryotoxic in some animals and so must not be used in pregnancy, and prolonged treatment should be avoided. Frequent monitoring of hepatic, renal, and bone marrow function is indicated during treatment. Albendazole is available as a gastrointestinal anthelmintic as a single 400 mg

treatment but does not have a product licence for the treatment of hydatid disease.

We are grateful to Dr John Morris (Bridgend General Hospital) and Professor Lennard Jones (the London Hospital) for allowing us to treat their patients, and to Dr D Cox, Dr H Skene-Smith, and the staff of the CT scanning unit, Queen Elizabeth Hospital, Birmingham.

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(Accepted 6 October 1982)

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Streptococcus pyogenes as probable cause of dysentery

Apart from *Staphylococcus aureus* no spherical bacteria are known to cause diarrhoea or dysentery.¹ I report a case of dysentery in which *Streptococcus pyogenes* was thought to be the causative organism.

Case report

A 54-year-old Caucasian woman developed colicky abdominal pain and diarrhoea with blood and mucus. A faecal specimen was liquid, consisting mostly of blood and mucus with only a small amount of faecal material. On microscopy no cyst, protozoa, ova, or helminths were seen but pus cells and red blood cells were plentiful. Selective culture procedures for all probable enteric pathogens (*Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*, and *Staphylococcus aureus*) yielded negative results. As she was still passing blood and mucus the possibility of a ruptured abscess in the rectum or gut was considered. The specimen was therefore cultured on routine non-selective blood-agar plates and incubated aerobically and anaerobically. This produced heavy growths of *Str pyogenes* (Lancefield group A) in almost pure cultures with a few colonies of *Escherichia coli*.

Another sample of faeces and a rectal swab were obtained on the fifth day of her illness and cultured on selective media and blood-agar plates as before. Both specimens produced heavy growths of *Str pyogenes* and no other pathogen on the blood-agar plates, while no pathogen was grown on the selective media; the identity of *Str pyogenes* was confirmed repeatedly using standard laboratory techniques.² The organism was sensitive to penicillin and erythromycin. She was given 1 MU benzylpenicillin intramuscularly followed by a 10-day course of phenoxymethylpenicillin and erythromycin, both 500 mg by mouth four times daily.

Throughout her illness she had no clinical signs or symptoms other than diarrhoea. Thorough clinical examination, including rectal and vaginal examinations, and detailed inquiries about contacts, foods, travel abroad, history of abdominal problems, and prior use of antibiotics did not yield any useful information on the cause or source of her illness. Blood counts, haemoglobin concentration, and erythrocyte sedimentation rate were within normal limits. Swabs from her nose, throat, axillas, inguinal regions, and vagina were cultured: the vaginal swab produced a light growth of *Str pyogenes* with a moderate amount of normal flora while the others grew only normal flora. Sera obtained on the fifth day of illness and 10 days later contained normal titres of antistreptolysin O antibody.

She started passing formed stools normal in appearance and frequency two days after beginning antibiotic treatment. She had no subsequent

abdominal discomfort or other complaint. Two further specimens of faeces, examined on the third and seventh day after the end of the course of antibiotics, appeared normal in naked-eye and microscopic examinations and did not grow *Str pyogenes* or any other pathogen. Swabs from various sites, as obtained before, were also cultured at the end of treatment; none grew any pathogen. At follow-up five months later she was well.

Comment

Enteric pathogens were never isolated in this case, and the epidemiological history did not support the possibility of infection from such pathogens. Thus the repeated isolation of *Str pyogenes* from the patient's faeces and rectal swab suggested that this organism was probably associated with the illness. Furthermore, clinical and bacteriological cures were achieved simultaneously when she was treated with the antibiotics to which *Str pyogenes* was sensitive. The usual practice of culturing stools on selective media did not grow *Str pyogenes*, and the diagnosis would have been missed if blood-agar media had not been used.

Despite an extensive search I have not found any other report of diarrhoea or dysentery caused by this organism. The source of infection in this case could not be established. The organism colonised the vagina and gut leaving the nose and throat free, but such colonisation is not particularly uncommon.^{3,4} The absence of signs or symptoms of systemic illness and the normal white cell count and antistreptolysin O titres excluded blood-borne infection. Normally either penicillin or erythromycin would be chosen for *Str pyogenes* infections, but in this case both were prescribed because of uncertainty of their effect on this organism in the gut.

I am grateful to Dr S Head, general practitioner, and to the laboratory staff for their co-operation in the investigations and management of this patient.

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(Accepted 29 September 1982)

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Severe hypophosphataemia in T-cell lymphoblastic lymphoma

In the treatment of lymphoma or leukaemia the metabolic derangements accompanying tumour lysis include potentially fatal hyperkalaemia or hyperphosphataemia, hypocalcaemia, and hyperuricaemia, complicated in some instances by renal failure.¹

We report an unusual patient with T-cell lymphoblastic lymphoma in whom recurrent symptomatic hypophosphataemia occurred in parallel with an increase in tumour burden and chemotherapy was accompanied by predictable episodes of hyperphosphataemia and hypocalcaemia.

Case report

A 26-year-old woman presented with a two-week history of generalised malaise, easy bruising, and menorrhagia. Examination disclosed, besides widespread ecchymoses and nodular skin infiltrates, generalised lymphadenopathy and hepatosplenomegaly. Results of investigations were: haemoglobin concentration 13.3 g/dl, white cell count $100 \times 10^9/l$ (90% lymphoblasts), platelet count $30 \times 10^9/l$. The chest radiograph showed massive anterior mediastinal lymph-node enlargement, and biopsy findings of the skin nodules and cervical nodes were consistent with lymphoblastic

lymphoma. Immunological characterisation of this tissue, together with peripheral blood lymphoblasts, confirmed the diagnosis of T-cell lymphoblastic lymphoma. Serum biochemical values were: urate 0.76 mmol/l (12.8 mg/100 ml), creatinine 130.0 μ mol/l (1.5 mg/100 ml), calcium 2.52 mmol/l (10.1 mg/100 ml), phosphate 1.27 mmol/l (3.9 mg/100 ml), and lactate dehydrogenase 1694 U/l.

Treatment was begun with intravenous hydration, allopurinol, and combination chemotherapy (CHOP) with cyclophosphamide (750 mg/m²), adriamycin (50 mg/m²), vincristine (1.4 mg/m²), and prednisolone (60 mg/m²) on days 1 to 5. Twenty-four hours after chemotherapy the serum phosphate concentration was 3.36 mmol/l (10.4 mg/100 ml) and lactate dehydrogenase activity 2574 U/l. The lymphadenopathy and organ enlargement rapidly resolved over the ensuing week. CHOP was administered at monthly intervals but five months after presentation cranial irradiation together with intrathecal methotrexate were required because of symptomatic cerebral lymphomatous spread. Chemotherapy was changed to L-asparaginase (colaspase), 10 000 U/m², and cytosine arabinoside (cytarabine), 200 mg/m², on days 1 to 5, administered at monthly intervals. Recurrence in the central nervous system necessitating irradiation occurred 10 months after presentation, and chemotherapy was altered to a monthly CHOP and L-asparaginase regimen.

Sixteen months after diagnosis the patient complained of profound muscle weakness, arthralgia, perioral paraesthesia, and sensitivity of the teeth. Gross lymphadenopathy and hepatosplenomegaly were present. The table lists the pertinent haematological and biochemical findings. The most notable feature was the severe hypophosphataemia, and urinary phosphate was not detectable. After chemotherapy the typical features of the tumour lysis syndrome with hyperphosphataemia, hypocalcaemia, and renal insufficiency (table) occurred concomitantly with a rapid reduction of peripheral blood lymphoblasts; return of plasma phosphate concentrations to normal was accompanied by normal urinary phosphate excretion.

Peripheral blood metabolic changes in patient with T lymphoblastic lymphoma

	Days*					
	-7	0	+1	+2	+6	+23
Urea (mmol/l) (normal 2.0-8.5)	3.9	9.9	21.9	24.9	11.5	1.8
Creatinine (μ mol/l) (normal 40-120)	130.0	170.0	180.0	150.0	150.0	90.0
Calcium (mmol/l) (normal 2.0-2.60)	2.57	1.93	1.85	1.67	1.89	2.41
Phosphate (mmol/l) (normal 0.70-1.30)	0.24	<0.05	1.19	2.72	1.27	0.90
Lactate dehydrogenase (U/l) (normal 50-300)	370	1745	19 250	18 900	2739	191
Urate (mmol/l) (normal 0.11-0.44)	0.23	0.45	0.38	0.42	0.20	0.38
Parathyroid hormone (μ g/l) (normal <1.0)	—	—	17.0	18.0	4.4	0.8
Lymphoblasts ($\times 10^9/l$)	12 360	251 250	25 400	510	0	40

* Before or after chemotherapy administered on day 0.

Conversion: SI to traditional units—Urea: 1 mmol/l $\approx$ 6.0 mg/100 ml. Creatinine: 1 μ mol/l $\approx$ 0.01 mg/100 ml. Calcium: 1 mmol/l $\approx$ 4.0 mg/100 ml. Phosphate: 1 mmol/l $\approx$ 3.1 mg/100 ml. Urate: 1 mmol/l $\approx$ 16.8 mg/100 ml.

Over the next three months the patient regularly presented with symptoms reflecting profound hypophosphataemia; chemotherapy produced predictable hyperphosphataemia and hypocalcaemia on each occasion. Eighteen months after presentation she died of *Streptococcus viridans* meningitis and septicaemia during a period of neutropenia. Necropsy showed diffuse lymphoblastic lymphoma affecting liver, pancreas, spleen, small bowel, lungs, kidneys, and brain.

Comment

This patient had pronounced symptomatic hypophosphataemia without any of the common predisposing factors for phosphate depletion, including chronic diarrhoea.² Heparinised whole blood obtained during the period of hypophosphataemia was assayed immediately after venesection and incubation at 37°C and no differences in serial phosphate concentrations suggested that the observed hypophosphataemia was not simply an in-vitro effect. Although the metabolic sequelae of rapid tumour lysis, observed in our patient, are well documented,^{1,3} the profound antecedent hypophosphataemia must be either extremely rare or unrecognised, being previously described in only two patients with acute leukaemia.^{4,5}

The cause of the hypophosphataemia is obscure. Generally it occurs in association with pronounced degrees of leukocytosis, and both the redistribution of extracellular phosphate into rapidly dividing malignant cells together with the greatly increased neoplastic mass may be contributing factors. Its clinical importance lies in the recognition that hypophosphataemia under these circumstances does cause morbidity and appears to be a premonitory finding for chemotherapy-induced