Our results agree with those of Shapiro *et al* in dogs.¹⁶ They showed that the absorption and action of insulin added to dialysate were delayed. On the other hand, Poulsen *et al*¹⁷ observed only a small increase in plasma insulin in pigs when insulin was continuously infused into an empty peritoneal cavity. In their experiment, however, the total amount of insulin per kg of body weight was two to three times smaller than in our study and infused over 90 minutes instead of being injected as a bolus. Nevertheless, they also showed that the increase in plasma insulin concentration was, for the same amount of insulin infused, much higher when injected into the portal vein or into a peripheral vein than into the peritoneal cavity.¹⁷ In man our results agree with those of Shade *et al*,¹⁸ who reported a sharp increase in plasma insulin concentrations when insulin was injected intraperitoneally. They also observed that this increase was much higher after intraperitoneal than after subcutaneous insulin injection.

Intraperitoneal administration of insulin, which is preferred by patients undergoing CAPD, is now used routinely. Most dialysis units recommend adding insulin to the dialysate bags but such a technique carries the risk that insulin will be adsorbed to the surface of polyvinyl chloride containers.¹⁹ We prefer the direct administration of insulin through the catheter. Although the current method of administering insulin and dialysate at the same time has already improved blood glucose control in diabetics on CAPD, the results of our pharmacokinetics study suggest that it would probably be better, at least in the prandial period, not to dilute insulin in the dialysate but to inject insulin (followed by a small amount of a flush solution) into an empty peritoneal cavity. At each dialysate exchange, coinciding with the beginning of a meal, the new bag, although connected to the catheter, could be kept clamped for at least 30 minutes after the intraperitoneal insulin injection. The rapid insulin absorption would then help to control postprandial increases in blood glucose concentration. The effectiveness of this procedure in improving glucose control is under investigation in our department.

Nevertheless, studies in patients with and without renal insufficiency and the results of our study suggest that the intraperitoneal route may be an appropriate site for long-term insulin delivery by means of an artificial pancreas or a simpler device, as this route of administration may be more physiological, with the insulin being mainly absorbed through the portal system.²⁰

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SHORT REPORTS

Acute arthritis associated with *Clostridium difficile* colitis

Acute arthritis is well documented in association with gastrointestinal disease. We report the first case, to our knowledge, of arthritis complicating *Clostridium difficile*-associated antibiotic colitis.

Case report

A previously fit 45-year-old woman with no history of gastrointestinal or joint disease received a seven-day course of oral clindamycin (150 mg four times daily) for an infected finger. Within 24 hours of starting the antibiotic she experienced transient nausea and vomiting and watery diarrhoea 10-14 times a day, which persisted until admission 26 days later. Five days before admission her right knee and right ankle had become acutely swollen and painful.

On examination she was feverish (37.8°C) and the right knee was hot, red,

and tensely swollen, with restricted, painful movement. There was a small effusion in the right ankle, and the calf was oedematous but cool. Examination showed no other abnormality. Sigmoidoscopy showed red granular mucosa without ulceration or pseudomembrane, and the histological picture was non-specific inflammatory change. Stool culture grew *Cl difficile*, and neutralisable faecal enterotoxin was detected by its cytopathic effect in tissue culture. Faecal culture for other recognised enteric pathogens, including campylobacter, was negative.

Aspiration of the knee produced a slightly turbid fluid (five neutrophils per high-power field) with no crystals detected under polarised light and negative Gram stain and culture. No cytopathic toxin was detected in the synovial fluid. Tests for rheumatoid factor, antinuclear factor, and HLA-B27 were negative, and plasma urate concentration was normal. No increase in viral antibody titres was detected, and a test for yersinia antibodies was negative. Radiography of the knee and ankle showed no bony abnormality. She was treated with oral metronidazole 400 mg thrice daily for seven days and aspirin 900 mg four times daily. The diarrhoea settled within two days, and after aspiration of 90 ml fluid from the knee the arthritis also improved. On discharge 10 days after admission bowel habit was normal, the rectal mucosa was macroscopically normal, and no faecal toxin was detectable. There was a small residual effusion in the knee with some stiffness but a full

range of movement. Follow-up for six weeks showed no bowel abnormality and minor residual swelling of the knee.

Comment

Reactive arthritis is common during infection with intestinal pathogens, including shigella, salmonella, yersinia, and campylobacter,¹ but *Cl difficile* has not been specifically linked with arthritis to date. Two case reports have described arthritis with antibiotic-associated diarrhoea but both were in the "pre-*Cl difficile*" era.^{2,3} The first was a case of migratory polyarthritis after clindamycin with histological pseudomembranous colitis in a 55-year-old man in whom all the large joints and two metacarpophalangeal joints were affected.² Both the diarrhoea and arthritis settled within six days after treatment with steroids. The second case was a 23-year-old woman with ampicillin-associated colitis and a monoarthritis of the right knee which settled within 14 days with aspirin, the diarrhoea having resolved five days earlier.³ The present case was similar in that the diarrhoea predated the arthritis, which improved rapidly after resolution of the diarrhoea. This case, however, documents the presence of faecal *Cl difficile* and its toxin, now the accepted pathogen in most cases of pseudomembranous colitis and in many cases of non-specific colitis and diarrhoea after antibiotics. In the absence of other causes for the acute arthritis this case possibly represents a true reactive arthritis to the presence of enteric *Cl difficile* infection, treatment with oral metronidazole resulting in rapid clearance of toxin and symptomatic relief.⁴

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Intrauterine vitamin D nutrition and postnatal growth in Asian infants

British Asians are at risk of vitamin D deficiency, especially during pregnancy.^{1,2} In a previous report² we showed that vitamin D supplements given to pregnant Asian women improved calcium status in the fetus in comparison with a placebo group. The infants have been followed since birth as part of a survey of growth and dentition in London Asians. This paper presents the results of measurements made on the infants in their first year, showing improved postnatal growth in those whose mothers received supplementary vitamin D.

Patients, methods, and results

A double-blind trial of vitamin D supplements in Asian women (ergocalciferol 1000 IU per day during the last trimester of pregnancy) was carried out in 1978-9.² Fifty-nine infants were born to women who had received supplementary vitamin D and 67 to the controls. There were no significant differences in birth weight, length, or head circumference in the two groups. The male:female ratio was 1.3:1 in both groups. The infants were seen at 3, 6, 9, and 12 months, when measurements were made of their naked weight on a well calibrated beam balance, crown-heel length on a horizontal stadiometer,³ and occipitofrontal head circumference. Postnatal vitamin supplements were not routinely given and breast-feeding was encouraged. The mean length of breast feeding was 3.2 months in the treated group, whose mothers had received vitamin D during pregnancy, and 3.5 months in the control group. These periods were not significantly different. Six infants in the treated group and three in the control group moved to another area and were lost to follow-up before the measurements were completed.

The results are shown in the table. The treated infants were significantly heavier at each follow-up visit. Lengths were greater at each visit in the treated group but only significantly so at 9 and 12 months. There was no significant difference in head growth between the two groups.

Comment

Little is known about the effects of fetal vitamin D nutrition on subsequent growth, though it appears to affect dentition.⁴ Our control group had evidence of moderately severe vitamin D deficiency,² but it had no apparent effect on intrauterine growth. The finding that these infants grew less well than the supplemented infants during their first year was therefore unexpected but presumably reflects the relatively prolonged action of the vitamin and the benefits provided by increased stores, rather than an unidentified growth-promoting effect. The greater influence on weight gain than on linear growth is unexplained; nevertheless, by 1 year of age crown-heel length in the treated group was 1 cm above the mean of our longitudinal growth data for Asians.⁵ We cannot exclude the possibility that the treated group were given better postnatal nutrition than the control group, but there seems no reason to suppose that this was so, and all the follow-up visits were conducted without knowledge of the original trial status of the mother and infant, which might subconsciously have influenced mothering. The results provide further support for the need to give vitamin D supplements to Asian infants prenatally and probably postnatally as well.

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Measurements of physical growth during first year of life in 53 Asian infants receiving antenatal vitamin D supplements and in 64 controls. Results are means $\pm$ SD

Age	Weight (kg)			Length (cm)			Head circumference (cm)		
	Treated	Control	p	Treated	Control	p	Treated	Control	p
Birth	3.13 $\pm$ 0.49	3.05 $\pm$ 0.51	NS	49.9 $\pm$ 2.5	49.6 $\pm$ 2.8	NS	34.6 $\pm$ 1.5	34.2 $\pm$ 1.7	NS
3 months	5.65 $\pm$ 0.58	5.40 $\pm$ 0.54	< 0.05	60.7 $\pm$ 2.1	60.0 $\pm$ 2.5	NS	40.2 $\pm$ 1.4	39.8 $\pm$ 1.5	NS
6 months	7.56 $\pm$ 0.60	7.09 $\pm$ 0.59	< 0.001	67.1 $\pm$ 2.3	66.6 $\pm$ 2.5	NS	43.0 $\pm$ 1.3	42.8 $\pm$ 1.7	NS
9 months	8.54 $\pm$ 0.59	8.29 $\pm$ 0.57	< 0.05	72.0 $\pm$ 2.3	71.2 $\pm$ 2.2	< 0.05	45.0 $\pm$ 1.5	44.8 $\pm$ 1.8	NS
12 months	9.39 $\pm$ 0.66	8.98 $\pm$ 0.62	< 0.001	76.2 $\pm$ 1.9	74.6 $\pm$ 1.7	< 0.001	45.9 $\pm$ 1.6	45.7 $\pm$ 1.4	NS
Increments over 0-12 months	6.39 $\pm$ 0.78	5.92 $\pm$ 0.92	< 0.01	27.9 $\pm$ 2.0	24.6 $\pm$ 5.7	< 0.001			