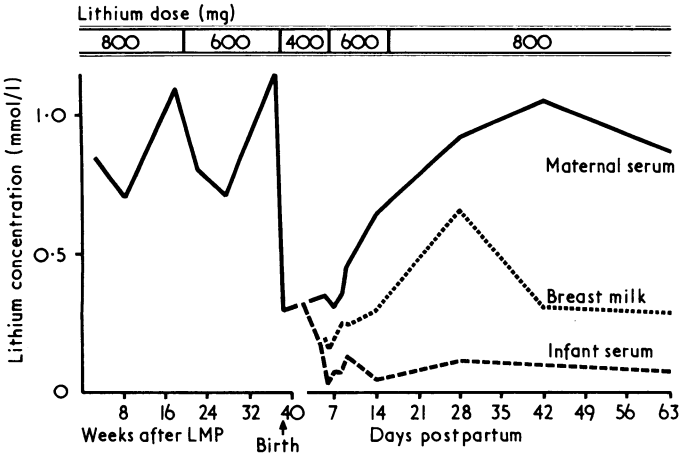
Lithium carbonate and breast-feeding

Lithium carbonate taken during pregnancy has been associated with neonatal hypotonia[1] and congenital heart disease.[2] There is little information on lithium concentrations in human breast milk or in the serum of breast-fed infants. We have studied such a case.

Case report

A 36-year-old woman, gravida 1, para 0+1, had been taking lithium carbonate for manic depressive psychosis for seven years when pregnancy was confirmed at eight weeks. The pregnancy was allowed to continue. Initially maintained at 800 mg daily, the dose was reduced twice during pregnancy to maintain therapeutic serum levels (see figure). Her mood was more stable than at any previous time, and she needed no other medication apart from routine haematinics. At 38 weeks she went into spontaneous labour lasting 12 hours and received protective forceps for suspected prematurity.



Concentration of lithium in maternal serum and milk and in infant serum.

Six hours before delivery she was given pethidine hydrochloride (Pethilorfan) 100 mg and promazine hydrochloride 50 mg. A boy was born weighing 3450 g. He was mildly hypotonic for the first two days. An electrocardiogram showed nothing abnormal, and the blood count and blood sugar level were normal; the lower femoral epiphysis was present.

The mother was anxious to breast-feed and this was established within six days. Lithium concentrations in the serum of the mother's pooled breast milk and the baby's urine were all monitored closely. The mother's serum level fell over the time of delivery, and the oral dose was doubled to achieve satisfactory serum levels. The baby's level was similar to the mother's at delivery but fell rapidly to 0·030 mmol/l by the sixth day and then rose slightly once breast-feeding was established. Despite a considerable rise in the mother's serum and breast milk levels there was no appreciable rise in the baby's serum level. He thrived and developed normally. Serial 12-hour collections of his urine on days six to nine inclusive gave lithium concentrations of 0·57, 1·20, 0·45, 0·64, 0·29, 0·30, 0·63, and 0·50 mmol/l. The mother became less anxious to breast-feed and stopped during the tenth week. Tests of thyroid function and bone chemistry were then normal.

Comment

The similar serum lithium levels for mother and baby at delivery confirmed that there is free exchange across the placenta.[3] The baby's serum level of lithium fell rapidly in the first week of life as reported.[3] The mean urinary concentration was 0·57 mmol/l, which was almost 10 times the mean serum level, and this shows that the neonatal kidney is capable of excreting lithium against a concentration gradient. Breast-milk lithium levels were about half maternal serum levels and rose with an increase in the oral dose. Despite the rise in concentration achieved in breast milk, the baby's serum levels remained constantly low—much lower than the level to which he had been exposed during pregnancy. Breast-feeding was discouraged and finally stopped at 10 weeks because of the known inhibition by lithium of cyclic 3'5' adenosine monophosphate[4] and the theoretical risk to the developing brain.

Since the mother was being treated for manic depressive psychosis we thought that the act of breast-feeding might be therapeutic. The baby will require further close follow-up, but the benefits from breast-feeding appeared to outweigh any possible risk from lithium in the neonatal period.

We thank Sister L Curtis, Mrs A Sanderson, and the biochemistry laboratory for their help.

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Meningitis caused by group R haemolytic streptococci

We report a case of meningitis caused by infection with group R haemolytic streptococci, probably the first case to be described in Britain.

Case report

A 62-year-old man cut his hand while operating a machine smeared with bacon fat at a pork pie factory. That evening he felt unwell, began to sweat, and developed rigors. Next morning he complained of pain in both hips, and was admitted to a local cottage hospital. The same day he became drowsy and developed meningism. He was transferred to the district general hospital. Lumbar puncture confirmed bacterial meningitis (white cell count $1{\cdot}5 \times 10^9$/l (1500/mm^3), mainly neutrophils, with Gram-positive diplococci, proteins 2·1 g/l (210 mg/100 ml), and glucose 2·69 mmol/l (48 mg/100 ml)). Culture of the cerebrospinal fluid grew a beta-haemolytic streptococcus on blood agar. The organism was resistant to bacitracin and grew on MacConkey's medium. The isolate could not be grouped with antisera for groups A, B, C, D, E, F, or G streptococci. The Cross-infection Reference Laboratory reported the organism to be a member of group R which had failed to grow in the presence of 10% bile or 4% NaCl at pH 9·6 or at 45°C and did not resist heat at 60°C for 30 minutes. Arginine and esculin were hyrdolysed, the Voges-Proskauer test result was negative, and polysaccharide was not formed from sucrose. Acid was produced from trehalose, lactose, raffinose, salicin, inulin, sucrose, and melibiose but not from sorbitol, mannitol, arabinose, melezitose, or dulcitol after five days. A similar organism was isolated from the blood. Purulent fluid was aspirated from the left hip joint, but no organism was cultured probably because the patient had already received several doses of penicillin.

He was treated with penicillin G 10 000 units intrathecally and 2 million units intravenously every two hours for the first 12 hours, then 1 million units intravenously four hourly for seven days. He improved considerably within 48 hours of starting treatment. His final recovery was complicated by a deep vein thrombosis. On discharge from hospital the only residua were high-tone deafness in the left ear associated with some vertigo.

Discussion

Haemolytic streptococci were implicated in septicaemic infections in pigs in 1954 by Field *et al*[1] and by de Moor[2] in 1959. They continued to be isolated from pigs and piglets in England and elsewhere in Europe. In Denmark in 1968 Perch *et al*[3] recorded two cases of

meningitis and one of septicaemia in man caused by haemolytic streptococci. Further strains have been isolated from man by several workers, and Kloppenburg *et al*[4] drew attention to the fact that all 15 reported cases had occurred in the Netherlands or Denmark and nearly all were of purulent meningitis. One patient kept pigs on his own premises for future processing in the factory, and the actual source of his infection was not identified. The incubation period, however, indicated that infection had resulted from his injury. Swabs from the machine and other apparatus at the factory were unobtainable and swabs from the patient's hand wound taken the day after admission failed to grow streptococci. Most previous cases have resulted from an infected wound. Purulent arthritis is a well known complication of group R streptococcal infection in pigs but as yet has not been recorded in man. Unfortunately our patient's hip was aspirated too late in the course of his illness to isolate the infecting organism, which was presumably a streptococcus.

We thank the staff of the Public Health Laboratory, Gloucester, for the initial investigations, the staff of the Cross-infection Reference Laboratory, Central Public Health Laboratory, Colindale, London, for specialist advice, and Dr R F Jarrett for permission to report this case. The case reported here is referred to by Windsor and Elliott[5] in a footnote to their paper on streptococcal infection in young pigs.

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Low molecular weight dextran: a continuing cause of acute renal failure

Low molecular weight dextran (LMWD), though not usually considered to be highly nephrotoxic, may precipitate acute renal failure (ARF) in certain conditions.[1] It may be the commonest cause of drug-induced ARF. Seven out of eight cases of drug-induced ARF referred to this unit from several hospitals during a recent eight-month period were caused by LMWD (10% dextran 40 in six cases and 6% dextran 70 in one case). All seven patients had ischaemic disorders.

Case histories

The case histories of patients are summarised in the table. In none could any cause other than LMWD be found for the ARF. All had widespread arterial disease and possibly such patients are particularly sensitive to the nephrotoxic effects of LMWD. In every case the onset of renal failure was relatively slow with a progressive decline in urine volume over three to six days. This was well illustrated by case 2, whose sequential daily urine volumes from the start of LMWD treatment were (in ml) 1900, 1000, 800, 650, 155, 0. Circulatory overload developed during this period.

Despite the decline in urine output LMWD was not withdrawn from any of the patients, and five developed complete anuria. During recovery there was not, as in many cases of ARF, a rapid diuresis but a slow rise in urine volume of 100-300 ml/day. Only two patients (3 and 6) achieved a diuresis of greater than 2 l/day. Dextran did not help the primary condition of any of the patients.

Comment

Dextrans of molecular weights below 60 000 easily filter through the glomerulus. They may accumulate in proximal tubular cells giving the swollen, vacuolated appearance of "osmotic nephropathy," although this appearance does not correlate with changes in renal function.[2] The high viscosity of concentrated dextran probably causes renal dysfunction by tubular plugging.[3 4] Damage is more likely to occur when renal perfusion is reduced[3 4]—a probable factor in cases 2, 4, and 7—or if renal damage is already present,[1] as in patients 2 and 6. Maintenance of diuresis with fluids and diuretics may protect the kidneys[3] and may have prevented the need for dialysis in cases 4 and 6, who were referred and treated before anuria occurred.

Except in cases 1 and 5 the total dosage of LMWD was within the accepted therapeutic range, but treatment was continued despite falling urine volumes. The occurrence of anuria with 6% dextran 70 in patient 7 is unusual, as only a small proportion of the dextrans in this solution are filtered through the glomerulus.

The uses of LMWD are limited. When it is indicated its propensity to cause ARF should be remembered and the following therapeutic rules observed[5]: (1) do not infuse faster than 1 l/day; (2) do not give if the urine output is below 1500 ml/day; (3) withdraw if the specific gravity of the urine rises above 1045; (4) do not give if the blood urea is above 10 mmol/l (60 mg/100 ml). A reduced urine output indicates that LMWD should be withdrawn and diuresis induced with diuretics and a high fluid intake.

Strict adherence to these rules would probably have prevented all the cases of LMWD-induced renal failure reported here.

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Case histories of seven patients with acute renal failure after administration of low molecular weight dextran

Case No	Age	Sex	Primary diagnosis	Dose of 10% dextran 40	Initial plasma urea concentration (mmol/l)	Initial urine volume (ml/day)	Duration of decline	Duration of complete anuria	Type and duration of dialysis	Comment
1	72	F	Diabetic gangrene of left foot	4 l in 2 days	Not measured	Not measured	3 days	28 days	Peritoneal; 4 weeks	Leg amputated after ARF
2	54	F	Ischaemic left leg, mesenteric ischaemia	3·5 l in 3 days	17·5	1900	6 days	11 days	Peritoneal; 15 days	Chronic pyelonephritis. Leg recovered
3	86	F	Ischaemic right foot	5 l in 5 days	8	Not measured	6 days	3 days	Peritoneal; 6 days	Foot improved after phenol sympathetic block
4	78	F	Left brachial embolus	2 l in 2 days	7·5	1000	3 days	12 hrs	Not needed	Embolectomy under local analgesia. Early treatment with frusemide
5	57	M	Left popliteal embolus	6 l in 5 days	Not measured	Not measured	6 days	14 days	Peritoneal and haemodialysis	Leg amputated after ARF. Died of pneumonia and disseminated intravascular coagulation
6	73	M	Diabetic gangrene of left foot	5·5 l in 5 days	21·9	1500	6 days	≥450 ml/day	Not needed	Amputation after renal recovery. Early frusemide treatment
7	70	M	Polycythaemia. Ischaemic left foot	5 l in 5 days*	Not measured	Not measured	5 days	6 days	Haemodialysis; 7 days	Some recovery of foot

*Dose refers to 6% dextran 70. ARF = acute renal failure. *Conversion: SI to traditional units*—plasma urea: 1 mmol/l ≈ 6 mg/100 ml.