returned within one day (cases 1 and 2) and 10 days (case 4). In addition, two patients (cases 2 and 3) almost lost their sweats when taking cimetidine. This is a preliminary report. Further investigations, including a randomised double-blind trial (which we are now doing), are required before this drug can be generally recommended for pruritus in Hodgkin's disease.

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Clearance of bacteriuria on discontinuing oral contraception

Bacteriuria in adult women may clear spontaneously or with antimicrobial therapy, but the factors influencing its clearance are not well understood. We present here data suggesting that among bacteriuric women who take oral contraceptives clearance is related to discontinuation of the medication.

Patients, methods, and results

In a community survey in 1973¹ 289 out of the 8352 women who participated were bacteriuric. Of these bacteriuric women the 12 premenopausal current oral contraceptive users between 16 and 49 years of age form the basis of this report. Follow-up surveys were done in 1974 and 1976. At each visit bacteriuria was defined by the presence of $\geq 10^5$ Gram-negative bacilli/ml urine on three consecutive cultures over a three-week period—except in 1974, when only two cultures were obtained. All women who were bacteriuric in the 1973 survey, including those who took oral contraceptives, were randomly assigned either to treatment by their own physicians or treatment in a special urinary tract infection clinic. Fisher's exact test was used to determine the significance of the relation between clearance of bacteriuria and discontinuation of oral contraceptives.

Eleven of the 12 oral contraceptive users who were bacteriuric in 1973 were visited at the follow-up survey one year later. Seven had stopped taking oral contraceptives and four had continued. None of the seven women who had stopped were bacteriuric while three of the four who had continued remained bacteriuric ($p=0.025$). Ten of these women had follow-up visits in the 1976 survey. None of the seven women who had discontinued oral contraceptives between 1973 and 1974 was bacteriuric in 1976, whereas two of the three bacteriuric women continuing to take oral contraceptives in 1974 were bacteriuric in 1976 ($p=0.067$).

Comment

These data indicate that clearance of bacteriuria in women who take oral contraceptives is related to discontinuation of the pill. We could find no other differences between the women who stopped taking oral contraceptives and those who continued which might account for the clearance of bacteriuria. The two groups were similar in age, parity, marital status, history of previous urinary tract infections, presence of symptoms referable to the urinary tract, and assignment to treatment. Estimates from population-based studies are that infection clears spontaneously in 25% of bacteriuric women each year. The features differentiating women likely to have recurring or persisting infection from those likely to have remission of the bacteriuria are not fully understood.^{2,3} Few specific factors have

been shown to influence clearance of bacteriuria. Recurrent infections seem to be more common in older women.³ The results in some but not all investigations suggest that localisation of infection to the kidneys rather than to the lower urinary tract is strongly associated with persistent or recurrent infection.

Previous reports^{4,5} have suggested an association between oral contraceptives and bacteriuria. Although both oestrogens and progestins alter urinary tract motility, and oestrogen administration appears to increase susceptibility to urinary tract infections in animals, the biological basis of the association remains unclear. Whatever the mechanism, the clearing of bacteriuria among women who discontinued oral contraceptives between two surveys one year apart implies reversibility.

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Non-haemolytic adverse reaction after transfusion of a blood unit containing penicillin

We have reported the presence of penicillinase-sensitive penicillins in blood units collected from voluntary donors.¹ Since minute amounts of penicillin can induce reactions in allergic patients,^{2,3} this finding suggested a possible relation between blood units containing penicillin and unexplained non-haemolytic adverse reactions after transfusion. We report such a reaction after transfusion of a blood unit containing penicillin.

Case report

A 20-year-old man with hydrocephalus caused by aqueduct stenosis was admitted several times to the department of neurosurgery. On his first admission a ventricular-peritoneal shunt was implanted, which later required multiple revisions. During another admission he developed a rash after an injection of benzylpenicillin and was diagnosed as being allergic to penicillin.

The present admission was because of obstruction of the drainage system, and it was decided to revise the shunt. He was given a prophylactic injection of 1 g cephazolin, and a ventricular-pleural shunt was implanted. A few hours later he developed a maculopapular eruption on the chest and limbs, pruritus, and fever (38°C). These symptoms were thought to be caused by hypersensitivity to the cephazolin and disappeared after 24 hours. Three days later the shunt had to be further revised. At the end of the operation he was given a transfusion of one unit of blood and again developed a maculopapular eruption on the chest, back, and limbs. The transfusion was stopped and the blood unit returned to the blood bank. The rash was again associated with fever (38.2°C) and pruritus; all symptoms disappeared after 36 hours.

No mismatch was found after repeated typing of both the patient's blood and the donor unit, or after repeat cross-matching and a direct antiglobulin test; an IgA deficiency was also excluded.⁴ The blood unit was tested for the presence of penicillin by bioassay.¹ A penicillinase-sensitive penicillin was found at a concentration equivalent to 2 µg benzylpenicillin/ml.

To confirm the hypersensitivity to penicillin the patient's serum was tested by the rat mast-cell degranulation technique.⁵ A cytopathic effect was observed in half of the mast cells tested with the patient's serum; normal serum from controls produced cytological alteration in only 1-6% of cells.

Comment

In this case conventional investigations⁴ did not show any aetiological cause for the patient's adverse reaction, but a penicillinase-sensitive penicillin was detected in the donor blood unit.

The patient's history, the symptoms that appeared after the injection of cephazolin, and the results of the rat mast-cell degranulation test leave little doubt about the diagnosis of hypersensitivity to the β -lactam antibiotics. The symptoms appearing after the transfusion of the blood unit containing penicillin were identical with those observed after the injection of cephazolin and consistent with an allergic reaction to penicillin.^{2,3} These findings indicate that the reaction in our patient was related to the presence of penicillin in the transfused blood unit.

Screening of donors at our blood bank includes questioning about the use of drugs. This case shows that this method is not reliable enough and that the presence of penicillins in blood units might induce reactions after transfusion. We suggest that blood units are tested for penicillins, especially when the recipient is known to be allergic to them. Testing is also warranted when conventional methods fail to show any reason for an adverse reaction after transfusion.

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Weight gain between dialyses in diabetics: possible significance of raised intracellular sodium content

Although well-timed renal transplantation, preferably using living related donors, offers the best chance of survival for diabetic patients who develop renal failure¹ regular haemodialysis (RDT) remains a valuable holding therapy. Diabetic patients on RDT face numerous problems,² including difficulty in obtaining reliable access to the circulation and increased prevalence of sepsis related to shunts and fistulae. These patients also gain excessive weight between dialyses² and, because of commonly-associated autonomic neuropathy, the ultrafiltration required with dialysis to correct this may cause undesirable hypotension. We have investigated weight gain between dialyses in a group of eight diabetic patients on RDT over a three-month period and compared them with a matched group of non-diabetic patients treated with RDT over the same period. After discovering grossly abnormal intracellular electrolyte concentrations in one of the diabetic patients we also studied leucocyte intracellular sodium content in a group of diabetic patients on RDT and peritoneal dialysis and compared them with a matched group of non-diabetic uraemic patients also on RDT. Six of the patients from the first part of the study were included in the second part.

Patients, methods, and results

The increase in weight between successive dialyses, separated by two to three days, was recorded over a three-month period. This was then expressed as a percentage of the patient's weight at the end of the previous dialysis and the mean obtained by dividing the total by the number of dialyses. Eight diabetic patients and eight non-diabetics were not significantly different in mean age, number of square metre hours of dialysis per week, urine output, or diuretic therapy. There was, however, a significantly greater

interdialytic weight gain in the diabetic group (4.6% of body weight compared with 2.4%, $p < 0.01$). Intracellular sodium content was measured on peripheral blood leucocytes obtained immediately before dialysis. Leucocytes were separated from about 30 ml venous blood by the method of Baron and Ahmed,³ involving dextran sedimentation of erythrocytes. Trapped extracellular fluid was measured using a ⁵¹Cr EDTA marker. After isolation cells were dried at 100°C to constant weight, treated with 0.1N HNO₃, and electrolyte concentrations determined by flame photometry. Eight diabetic patients who had been on regular dialysis for at least three months, including two patients on peritoneal dialysis, were compared with eight non-diabetics on maintenance haemodialysis. The patients were matched in the same way as in the first group, and in particular there was no significant difference in sodium intake or serum albumin concentration between the two groups. A significantly higher intracellular sodium was found in the diabetic patients (mean $\pm$ SD = 143.4 $\pm$ 68.6 mmol/kg dry cell weight v 76.2 $\pm$ 30.3 mmol/kg, $p < 0.025$).

Comment

These observations confirm that the interdialytic weight increases in diabetics on dialysis, although this report is the first accurately to quantify this. High intracellular sodium content and concentration accompanied by a raised cell water and low intracellular potassium has been described in uraemia and ascribed to impairment of the ouabain-sensitive sodium pump. These abnormalities return to normal with regular dialysis therapy,⁵ but this has clearly not occurred in the diabetics we have studied since their intracellular sodiums remain high. It has been suggested that hyperglycaemia and possible high concentrations of circulating angiotensin and aldosterone are responsible for increased thirst and weight gain in diabetics on dialysis.² But our results suggest an alternative explanation, since possibly the high white cell sodium content may be mirrored in the central nervous system and acts as a "false signal" to the thirst centres. The failure of regular haemodialysis to reverse this abnormality in diabetics remains unexplained.

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Relapses in primate malaria: discovery of two populations of exoerythrocytic stages. Preliminary note

Shortt and Garnham's¹ discovery in 1948 of exoerythrocytic schizonts of *Plasmodium cynomolgi* in the liver of the rhesus monkey 102 days after the inoculation of sporozoites and just before the onset of a relapse led them to postulate that successive cycles of development in the liver were responsible for the "true" relapse. Further work (see review²) suggested that this idea was invalid, and the alternative theory of dormancy was substituted. In fact, in 1946 Shute³ had already suggested that the sporozoite, or "x body," into which it grew might remain inactive as a resting stage in the host. Apart from the nearly mature exoerythrocytic schizonts which have continued