our patients. Our results, however, indicate that conflicting reports^{2,3} about the diurnal rhythm of water and salt excretion in renal allograft recipients are explicable by the fact that the patients were studied at different times after transplantation. Although nocturia is common in renal failure, our results clearly show that renal failure alone cannot account for nocturia in patients who have recently undergone transplantation since these patients had significantly lower D:N ratios of urine volume than those with renal failure with comparable creatinine clearances ($p < 0.05$); the patient with the severest nocturia (case 1) had normal renal function; and the patients studied at least a year after transplantation had normal D:N ratios of urine volume, although their mean creatinine clearance was significantly lower than that in the normal subjects ($p < 0.01$). Other possible causes of the nocturia are discussed below.

Autonomic neuropathy—Autonomic dysfunction⁴ produces nocturnal polyuria and saluresis. It is tempting to postulate that autonomic dysfunction, which is common in patients receiving dialysis,⁵ might account for the nocturia in the first few months after transplantation and that as the allograft continues to function the autonomic dysfunction is corrected, thereby normalising water and salt excretion. None of our patients, however, had postural hypotension or other clinical signs of autonomic neuropathy, and the cardiovascular reflex in eight patients in the recent-transplant group as assessed by the Valsalva ratio was not significantly different from that in 42 healthy volunteers. While a normal Valsalva ratio probably excludes gross autonomic dysfunction, an abnormal ratio does not establish the presence of autonomic neuropathy, since the ratio is reduced in cardiac insufficiency.¹

Allograft positions—Although the allograft's position may have some unknown haemodynamic influence on its function, it cannot be responsible for the early nocturnal polyuria since the abnormality corrects itself with time while the kidney remains in the same position.

Influence of drugs—Since all our patients who had received transplants took prednisolone at 2000 the mineralocorticoid activity of the drug would be expected to reduce nocturnal sodium excretion, whereas the opposite was observed. The nocturnal kaliuresis in patients in the recent-transplant group

was probably caused by the combined effects of urine volume and steroids given at night.

Postural influence—The reported normal diurnal rhythm of water excretion in renal allograft recipients when the influence of posture has been eliminated⁶ suggests that the denervated kidney is unduly sensitive to postural changes. This is supported by our observation that when the patient in case 1 remained recumbent for 24 hours the nocturia was almost completely abolished (D:N urine-volume ratio changed from 0.35 to 0.90) while the dose of immunosuppressive drugs remained unaltered. It is not known why this supersensitivity to postural changes disappeared at least a year after transplantation, although gradual adaptation of the denervated vasculature is possible. Whether or not re-nerivation of the graft⁷ plays a part remains speculative.

Our study has shown that renal allograft recipients often have nocturia, which abates spontaneously, usually within a year after operation. It is not due to renal insufficiency, autonomic neuropathy, or immunosuppressive drugs but is related to postural influences. Patients who have received transplants and who complain of nocturia should be reassured that it will eventually disappear.

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SHORT REPORTS

Cimetidine for pruritus in Hodgkin's disease

Cimetidine is a potent histamine H_2 -receptor antagonist that has proved useful in digestive disorders with gastric-acid hypersecretion.¹ It has been used for pruritus related to cholestasis,² chronic renal failure,³ and myeloproliferative disorders.⁴ These reports have prompted us to try the drug in four cases of pruritus due to Hodgkin's disease.

Case reports

(1) A 24-year-old woman was admitted because of low back pain, weight loss, night sweats, and intense generalised pruritus. Biopsy of a left supraclavicular lymph node showed Hodgkin's disease, nodular sclerosing type. Staging laparotomy was not performed because of lymphographic abnormalities of the retroperitoneal nodes. Cimetidine by mouth was started at a dose of 1 g daily (200 mg at mealtimes three times a day, and 400 mg at bedtime). The pruritus completely disappeared within 24 hours. The itching returned within 12 hours when cimetidine was stopped and disappeared when it was restarted. Cimetidine was withdrawn when chemotherapy (MOPP regimen) was begun. Pruritus did not recur.

(2) A 19-year-old woman was referred to us because of enlarged cervical and mediastinal lymph nodes and a three-month history of lassitude, sweats, and generalised pruritus. Biopsy of a cervical node showed lymphocyte-depleted Hodgkin's disease. She was given cimetidine 1 g daily by mouth

(200 mg at mealtimes and 400 mg at bedtime). This dramatically reduced itching and sweats within one day. Pruritus and sweats returned within 12 hours when cimetidine was withdrawn.

(3) A 29-year-old woman with a six-month history of severe pruritus and night sweats was admitted with cervical and mediastinal lymphadenopathy. Biopsy of a cervical node showed nodular sclerosing Hodgkin's disease. We tried dexchlorpheniramine for the itching effect. Cimetidine by mouth 1 g daily (200 mg at mealtimes and 400 mg at bedtime) was given. Relief from the pruritus and sweats was progressive and complete within four days. Cimetidine was stopped, without any recurrence of itching, when the patient began a MOPP regimen.

(4) A 22-year-old woman was admitted for fever, sweats, pruritus, and cervical, axillary, and inguinal lymphadenopathy. Biopsy of an inguinal lymph node showed nodular sclerosing Hodgkin's disease. Four cycles of MOPP were given. Pruritus and fever reappeared soon after the fourth course of MOPP. Cimetidine 1 g daily by mouth (200 mg at mealtimes and 400 mg at bedtime) was started. Within four days her pruritus was completely relieved. Cimetidine was discontinued without immediate recurrence of itching. It was successfully resumed 10 days later for a recurrence of itching.

Comment

Severe generalised pruritus is not uncommon in Hodgkin's disease. Its pathogenesis is poorly understood, and treatment with systemic or topical medications is often disappointing. Itching was relieved in all our patients by cimetidine alone—within a day in two cases and after a few days in the other two. When treatment was stopped itching

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.