tressing neurological disorder. In either case, it would seem that this patient's brain stem activity had become set precariously and that the arrival of local anaesthetic caused its temporary breakdown.—We are, etc.,

Gerald Parsons-Smith
J. M. Norcliffe Roberts.


REFERENCE

Carbenicillin and Hypokalaemia

Sir.—Brunner and Frick1 drew attention to the development of hypokalaemia and metabolic alkalosis with high doses of benzylpenicillin therapy. Their patients received 60 g daily for periods of 10 to 14 days. The standard dose of carbenicillin (α-carboxybenzylpenicillin, Probenecid) for systemic pseudomonas infections is 30 g per 24 hours. No serious electrolyte disturbances have been recorded to date in patients receiving this antibiotic.2 However, we have seen recently two patients who developed hypokalaemic alkalosis with carbenicillin therapy and wish to draw attention to this potentially dangerous complication.

An 80-year-old woman fell sustaining an undisplaced peritrochanteric fracture of her left femur which was treated conservatively. Urinary retention occurred, requiring an indwelling catheter. Pseudomonas pyocyanea were cultured in pure growth from repeated specimens of urine. She became febrile, had marked anorexia, vomited from time to time, and developed a painful, red, swollen wrist suggestive of bacteremia although blood cultures proved sterile. Investigations: serum sodium 135, potassium 4·1, bicarbonate 27 mEq/L, urea 29 mg./100 ml. Two days later Carbenicillin 30 g./24 hrs. was given in two litres of normal saline in view of her dehydration. Five days later she had sacral oedema and a raised jugular venous pressure. The infusion volume was halved and bendrofluazide 5 mg per day given. The patient was afebrile a week later, and felt well, but was hypokalaemic: serum sodium 138, potassium 2·0, bicarbonate >30 mEq/L, ura 30 mg./100 ml. The carbenicillin was stopped and the hypokalaemia rapidly responded to oral potassium chloride.

A 12-year-old woman was involved in a road traffic accident sustaining a compound fracture of her left tibia and fibula with extensive soft tissue damage. An initial exploratory operation revealed injury to the anterior and posterior tibial arteries. The leg became infected and repeated swabs yielded pure cultures of Pseudomonas pyocyanea. The patient was afebrile with spikes of fever up to 104° F. (40° C.).

On 12 September carbenicillin was started, 5 g 4-hourly into a dextrose saline infusion. The next day an above knee amputation was performed. Carbenicillin was stopped on 21 September when the patient was complaining of lethargy and weakness and was found to have sluggish tendon reflexes. A day later investigations showed a severe hypokalaemic alkalosis: serum sodium 131, potassium 1·5, bicarbonate 40+ mEq/L, ura 10 mg./100 ml. Again oral potassium chloride in large doses rapidly corrected the electrolyte disorder.

In the first case bendrofluazide and a poor dietary intake may have been partly responsible for the hypokalaemia. In the second case there were no such contributory factors. The mechanism of penicillin-induced hypokalaemia is not certain, but probably depends on penicillin acting as a non-reabsorbable anion thus increasing passive distal tubular potassium excretion down an increased negative transtubular potential difference.3 Although carbenicillin contains 4·7 mEq of sodium per gram, an increased distal tubular sodium load is probably not generally an important factor as sodium delivery is only rate limiting for the hypothetical cation exchange mechanism in certain circumstances.4 However, both the above patients had other factors tending to reduce sodium excretion with probable increased aldosterone production. The first patient developed heart failure, was found to have a serum albumin of only 2·2 g./100 ml and was on phenylbutazone. The second patient had a general anaesthetic and surgery which are often followed by salt and water retention.4 Distal tubular sodium reabsorption may thus have been increased in both instances, encouraging tubular excretion of potassium especially in view of the relative deficiency of chloride ion.

The manufacturers recommend that for severe infections probenecid be used to increase blood levels of carbenicillin. Probenecid was not used in the present cases and might well have prevented hypokalaemia by reducing renal tubular levels of carbenicillin. As there is no preparation of probenecid for parenteral administration it is likely that carbenicillin will be used on many occasions by itself. Carbenicillin is a valuable drug in the treatment of pseudomonas infections which were cured in both our patients. However, on occasions it may give rise to dangerously severe hypokalaemia.—We are, etc.,

B. I. Hoffbrand
J. D. M. Stewart.

Whittington Hospital.
Archway, N.19.

REFERENCES
2 Price, J. D., personal communication.

Labelled Fibrinogen in Renal Transplantation

Sir.—Mr. J. R. Salaman (30 May, p. 517) has suggested that surface measurements may have particular value in recipients with delayed function of renal transplants in the first few weeks after transplantation, and that a percentage of transplant radioactivity of more than 120% of that of the heart would appear to indicate rejection.

We have performed similar studies in nine patients here,1 and have found that late transplant rejection is accompanied by surface accumulation of fibrinogen radioactivity. However, it was observed that during the early phase after transplantation it was the wound healing rather than rejection of the transplant that accounted for the increased radioactivity. Thus, the patient shown in Fig. 1 had a marked increase of radioactivity over the transplant although there was no evidence of rejection, and there was a similar increase in radioactivity over the nephrectomy wound of the other side. Although in the patient shown in Fig. 2 the control side, where the nephrectomy had been performed two years before transplantation, showed no increase of radioactivity, the increase over the transplanted side was most probably due to the process of wound healing, since there was no evidence of rejection. The bladder was emptied before each measurement and no haematomata were present. It may be noted (right half of both

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