defects appears to occur with special frequency, in which the aetiology may well be different. Many of these have been described by Robertson *et al.*¹⁶

There is no evidence either from the data in this paper or from other published reports that the risk of hydrocephalus after a male proband is different for male or female sibs or that there is any differential sex risk except in the special sex linked syndrome.

I conclude that after a baby with congenital hydrocephalus has been conceived there is a substantially higher, but still low, risk to brothers and sisters alike of having either hydrocephalus or neural tube defects. The risk that uncomplicated hydrocephalus will affect the siblings of children with neural tube defects is of the same order. Consequently the two conditions, at least in a large proportion of cases, is probably of the same aetiology, and the same considerations should therefore be given to their possible primary prevention and to the need for appropriate antenatal tests to detect and deal with them according to the merits of the case.

I wish to thank the Richard Fund of Sheffield for secretarial help.

References

- ¹ Lorber J. The family history of spina bifida cystica. *Pediatrics* 1965;35:589-95.
- ² Carter CO, David PA, Laurence KM. A family study of major central nervous system malformations in south Wales. *J Med Genet* 1968;5:81-106.
- ³ Carter CO, Roberts F. The risk of recurrence after two children with central nervous system malformations. *Lancet* 1967;i:306-8.

- ⁴ Smithells RW, Seller MJ, Harris R, *et al.* Further experience of vitamin supplementation for prevention of neural tube defect recurrences. *Lancet* 1983;ii:1027-31.
- ⁵ Office of Population Censuses and Surveys Monitor. *Congenital malformations*. London: HMSO, 1983. (MB3 83/5.)
- ⁶ Lorber J, De MC. Family history of congenital hydrocephalus. *Dev Med Child Neurol* 1970;suppl 22:94-100.
- ⁷ Edwards JH. The syndrome of sex-linked hydrocephalus. *Arch Dis Child* 1961;36:486-93.
- ⁸ Weatherall JAC. A review of some effects of recent medical practices in reducing the numbers of children born with congenital abnormalities. *Health Trends* 1982;14:85-8.
- ⁹ Nevin NC. Prevention of neural tube defects in an area of high incidence. In: Dobbing J, ed. *Prevention of spina bifida and other neural tube defects*. London: Academic Press, 1983:127-53.
- ¹⁰ Burton BK. Recurrence risks for congenital hydrocephalus. *Clin Genet* 1979;16:47-53.
- ¹¹ Adams C, Johnston WP, Nevin NC. Family study of congenital hydrocephalus. *Dev Med Child Neurol* 1982;24:493-8.
- ¹² Record RG, McKeown T. Congenital malformations of the central nervous system. II. Reproductive history and familial incidence. *British Journal of Social Medicine* 1950;4:26.
- ¹³ Borle A. Sur l'étiologie de l'hydrocéphalie congénitale à propos d'un cas d'hydrocéphalie concordant chez de jumeaux univitellins. *Journal of Human Genetics* 1953;2:157.
- ¹⁴ Gellman V. Congenital hydrocephalus in monovular twins. *Arch Dis Child* 1959;34:274.
- ¹⁵ Smithells RW, D'Arcy EE, McAllister EF. The outcome of pregnancies before and after the birth of infants with nervous system malformations. *Dev Med Child Neurol* 1968;15:6-10.
- ¹⁶ Robertson RD, Sarti DA, Brown WJ, Crandall BF. Congenital hydrocephalus in two pregnancies following the birth of a child with a neural tube defect: aetiology and management. *J Med Genet* 1981;18:105-7.
- ¹⁷ MacMahon B, Pugh TF, Ingalls TH. Anencephalus, spina bifida and hydrocephalus. *British Journal of Preventive and Social Medicine* 1953;7:211-9.
- ¹⁸ Williamson EM. Incidence and family aggregation of major congenital malformations of central nervous system. *J Med Genet* 1965;2:161-72.
- ¹⁹ Czeizel A, Revesz C. Major malformations of the central nervous system in Hungary. *British Journal of Preventive and Social Medicine* 1970;24:205-22.
- ²⁰ Bay C, Kerzin L, Hall BD. Recurrence risk in hydrocephalus. *Birth Defects* 1975;15(5c):95-105.
- ²¹ Howard FM, Till K, Carter CO. A family study of hydrocephalus resulting from aqueduct stenosis. *J Med Genet* 1981;18:252-5.

(Accepted 15 June 1984)

Comparison of reliability of tests to distinguish upper from lower urinary tract infection

G H C SCHARDIJN, L W STATIUS VAN EPS, W PAUW, C HOEFNAGEL, W J NOOYEN

Abstract

The results of scintiphotography with gallium-67 (⁶⁷Ga), renography with technetium-99m diethylene triamine penta-acetic acid, immunofluorescence of antibody coated bacteria, and determination of renal β_2 microglobulin excretion were compared in 19 patients with upper and 15 patients with lower urinary tract infection. All patients with acute pyelonephritis showed an appreciable unilateral or bilateral uptake of ⁶⁷Ga and an increased excretion of β_2 microglobulin, whereas immunofluorescence of antibody coated bacteria yielded positive results in only 10. In patients with lower urinary tract infections excretion of β_2 microglobulin and uptake of ⁶⁷Ga were always normal, whereas immunofluores-

cence of antibody coated bacteria was positive in three cases.

Scintiphotography with ⁶⁷Ga and determination of renal β_2 microglobulin excretion are currently the most reliable non-invasive methods of detecting acute pyelonephritis.

Introduction

About 20% of patients admitted to dialysis units with end stage kidney disease have a history of recurrent upper urinary tract infection.¹ Moreover, asymptomatic bacteriuria correlates with a shortened life expectancy. The problem of diagnosing and localising renal infection has challenged many clinicians, and many diagnostic procedures and methods have been suggested.² Bilateral ureteric catheterisation and bladder washout procedures are currently considered to be the most specific. These methods are, however, time consuming and have the risk of introducing new pathogenic micro-organisms. They may also produce false negative results in cases of obstructive uropathy or as a result of previously administered antibiotics. Intravenous urography is of limited value, especially in the case of acute pyelonephritis.³⁻⁵

Scintiphotography with gallium-67 (⁶⁷Ga) has been reported by several investigators as a useful method for diagnosing renal infections.⁶⁻¹⁰ We have reported that upper and lower urinary tract infections may be distinguished by estimating the excretion of urinary β_2 microglobulin.¹¹ False positive results may be obtained in patients with pre-existent tubular dysfunction and

Slotervaart Hospital, 1066 EC Amsterdam, The Netherlands

G H C SCHARDIJN, MD

L W STATIUS VAN EPS, head of department of internal medicine
W PAUW, microbiologist

Antoni van Leeuwenhoek Hospital, 1066 CX Amsterdam, The Netherlands

C A HOEFNAGEL, physician in nuclear medicine

W J NOOYEN, PHD, biochemist

Correspondence to: Dr L W Statius van Eps.

false negative results if the urinary pH is lower than 6. In the present study we compared the results of scintiphotography with ⁶⁷Ga, renography with technetium-99m (^{99m}Tc) diethylene triamine penta-acetic acid (DTPA), determination of renal excretion of β_2 microglobulin, and immunofluorescence of antibody coated bacteria in patients with acute pyelonephritis or lower urinary tract infection.

Subjects and methods

We studied 34 patients and 44 controls, all of whom had been admitted to hospital. Nineteen of the patients were suffering from acute pyelonephritis and 15 from a lower urinary tract infection. Only patients with urinary tract infections underwent scintiscanning with ⁶⁷Ga, but all patients and controls underwent intravenous urography. The controls had no signs of urinary tract infection or impaired renal function.

Acute pyelonephritis was diagnosed according to the following criteria: (1) clinical and physical findings typical of acute renal inflammation; (2) positive cultures of blood and urine with the same micro-organism; (3) abnormal results of intravenous urography—acute pyelonephritis can cause the following radiographic findings: dilated and distorted pelvicalyceal structures, non-obstructive ureteric dilatation, diminished concentration of contrast material, a delayed pyelogram, renal enlargement, and a prolonged or diminished visualisation of the kidney or kidneys; and (4) positive results of scintiphotography with ⁶⁷Ga. Only patients who met at least three of these criteria were considered to have pyelonephritis. Patients with lower urinary tract infection had a typical history of acute cystitis and yielded negative results to intravenous urography.

Scintiphotography with ⁶⁷Ga—⁶⁷Ga was given intravenously in a dose of 74 MBq (2 mCi). Posterior and anterior abdominal scans were obtained by collecting counts over five minutes in a 256 × 256 matrix 48 hours after injection and, in case of faint renal accumulation, again after 96 hours. A γ camera with a large field of view was used equipped with a medium energy collimator using three (93, 185, and 300 keV) of the four photopeaks of ⁶⁷Ga, being responsible for 41, 23, and 18% of the total counts respectively. Radioactivity over the heart or aorta as blood pools was used as the reference point. After scintiscanning with ⁶⁷Ga the patients were given 185 MBq (5 mCi) ^{99m}Tc DTPA intravenously, while lying in the same position. With the collimator adjusted, the energy peak of 140 keV was used for the renography. As the emission of gallium influences the curves of the technetium counts over the kidneys the images of the kidneys were of more importance than the curves for the assessment of the renal function and for the detection of postrenal obstruction. The analyses were done with an MDS A two system computer, which enabled us to mark the regions of interest. With this method, the kidney margins were projected over the accumulation of ⁶⁷Ga to ensure that the increased uptake of ⁶⁷Ga was actually localised in the kidneys.

Excretion of β_2 microglobulin— β_2 microglobulin was assayed by a solid phase radioimmunoassay (Pharmacia, Uppsala). We studied the stability of β_2 microglobulin under conditions of different urinary pH at a temperature of 37 °C. The estimation of β_2 microglobulin concentration in the urine was irreversibly influenced after incubation for two

hours at a pH lower than 11.¹ To prevent this we gave our patients 4 g sodium bicarbonate the evening before the experiment and another 4 g during the day on which urine was collected. Only specimens with pH $\geq$ 6 were assayed.

Immunofluorescence of antibody coated bacteria—Specimens of fresh midstream urine were spun at 4000 revolutions per minute for 10 minutes. The urine sediment was washed twice in a buffered sodium chloride solution pH 7.3, after which 0.2 ml fluorescein-conjugated antihuman immunoglobulin G of horse origin was added. Incubation was for 30 minutes at 37 °C. After incubation the urine sediment was washed twice again in the buffered saline solution. The urine was then investigated immediately with a fluorescence microscope with a magnification of $\times$ 400. Fluorescence was assessed on a five point scale varying from 0 (no fluorescence) to 4 (strong fluorescence). Furthermore, the result was considered to be positive if at least half, and borderline if at least a quarter, of the bacteria were coated with immunoglobulin.

Results

All patients with acute pyelonephritis yielded positive results to scintiphotography with ⁶⁷Ga and showed raised excretion of urinary β_2 microglobulin, whereas all patients with lower urinary tract infection yielded negative results to scintiphotography with ⁶⁷Ga and showed normal excretion of urinary β_2 microglobulin (table). There was no overlap in urinary excretion of β_2 microglobulin between patients with upper and those with lower urinary tract infection (fig 1).

FIG 1—Urinary excretion of β_2 microglobulin in 19 patients with acute pyelonephritis, 15 patients with lower urinary tract infections, and 44 controls.

Results of scintiphotography with ⁶⁷Ga, renography with ^{99m}Tc DTPA, immunofluorescence of antibody coated bacteria, and determination of urinary β_2 microglobulin excretion in three groups of subjects

	Patients with upper urinary tract infection (n = 19)	Patients with lower urinary tract infection (n = 15)	Controls (n = 44)
Mean (range) age (years)	68.9 (20-92)	67.5 (22-88)	54.7 (20-70)
Mean (range) urinary β_2 microglobulin (μ g/24 h)	8.569 (4.89-60.000)	162 (33-308)	110 (33-361)
Mean (range) urinary β_2 microglobulin/creatinine (μ g/mmol)	1.587 (69-7792)	23.1 (5-43.6)	13.5 (4.8-33.5)
No of patients in whom ⁶⁷ Ga scintiphotography was:			
Positive	19		
Negative		15	
No of subjects in whom immunofluorescence of antibody coated bacteria was:			
Positive	7	3	1
Borderline	3	1	1
Negative	9	11	42

Immunofluorescence of antibody coated bacteria yielded positive results in only 10 patients with acute pyelonephritis, whereas three patients with lower urinary tract infection and one of the controls yielded a definite positive result. In several patients with upper urinary tract infection an increased uptake of ⁶⁷Ga was accompanied by a decreased visualisation of ^{99m}Tc DTPA, suggesting decreased function of the inflamed kidney (fig 2) partially explained by a diminished renal blood flow. Moreover, the delayed renal localisation of ⁶⁷Ga correlates well in most patients with unilateral pyelonephritis with overt tenderness of the renal region.

Discussion

^{67}Ga is currently used widely in localising tumours and detecting infectious lesions, particularly abscesses. It is a γ emitting radionuclide with a physical half life of 72 hours. After injection it is bound to plasma transferrin, polymorphonuclear leucocytes, and lymphocytes. Binding to erythrocytes is negligible.¹² It is transported to the whole body, and high concentrations are found in the liver, spleen, skeleton, kidneys, and intestine.

The reason for the high concentration of ^{67}Ga in inflammatory lesions is still not certain. It may be explained by an increased affinity of ^{67}Ga to polymorphonuclear leucocytes, lymphocytes, bacteria, or acute phase proteins like lactoferrin.¹²⁻¹⁵ An abnormal renal retention of ^{67}Ga has been documented in pyelonephritis, Wegener granulomatosis, vasculitis, renal vein thrombosis, renal and perinephric abscesses, primary renal

nucleated cells and is part of the HLA complex on the cell surface. The daily production is constant in healthy subjects and increased in many diseases, especially in those accompanied by activation of lymphocytes. The small molecule, which leaves the body exclusively by glomerular filtration, is filtered easily through the glomerular membrane, almost completely reabsorbed (99.9%), and metabolised by the proximal tubule. In proximal tubular dysfunction, like pyelonephritis, the reabsorption of β_2 microglobulin is disturbed. As a consequence, the renal excretion of β_2 microglobulin is increased ($>370 \mu\text{g}/24 \text{ h}$) and returns to normal when the tubular function improves—for example, during treatment of the infection with appropriate antibiotics. Special precautions should be taken to avoid the production of urine with a pH lower than 6 as β_2 microglobulin loses its antigenicity irreversibly in urine with a pH lower than 6, even in the short period before voiding. Our results confirm the value of

FIG 2—Results of isotope scanning in an 81 year old man with pyelonephritis of the right kidney and urosepsis caused by *Escherichia coli*, showing (left) intense accumulation of ^{67}Ga in the upper pole of the right kidney accompanied (right) by decreased activity of ^{99}Tc DTPA over the same region and a delayed excretion of ^{99}Tc DTPA of the right kidney. (Posterior view in all cases.)

tumours, amyloidosis, and sometimes in non-infectious interstitial nephritis.^{8 16-18}

Ormrod *et al* found an increased uptake of ^{67}Ga in the kidneys of rats with experimental unilateral pyelonephritis caused by a direct inoculation with *Escherichia coli*.¹⁹ The accumulation of ^{67}Ga correlated well with gross and histopathological findings in the pyelonephritic kidneys. The ^{67}Ga activity over these kidneys increased throughout the first seven days, but there was no significant difference in activity between 14 and 28 days.

We found an increased accumulation of ^{67}Ga in all patients with acute pyelonephritis. In several patients with unilateral pyelonephritis the increased uptake of ^{67}Ga was accompanied by a decreased activity of ^{99}Tc DTPA over the same kidney, while the contralateral kidney that was not affected yielded normal results to renography without an increased uptake of ^{67}Ga . Our findings are similar to those of Biskjaer *et al*²⁰ and Handmaker,¹⁰ who observed in several patients with pyelonephritis a decreased renal radioactivity using renal cortical radiopharmaceutical agents like ^{99}Tc succimer or ^{99}Tc glucoheptate. Handmaker suggested that these observations can be explained by peritubular oedema, increased interstitial pressure, and plugs of cellular debris within the tubules as were found in pyelonephritis.¹⁰

β_2 microglobulin is a protein with a light molecular weight (11 800 daltons). It is produced by the ribosomes of most

determining excretion of β_2 microglobulin to diagnose acute renal infections. Moreover, follow up studies can be used to control the efficacy of drug treatment and to detect recurrences.

In 1974 Thomas *et al* showed the binding of antibodies on the surface of bacteria with a direct immunofluorescence test.²¹ They found a correlation between a positive result to the test and upper urinary tract infection and between a negative result and lower urinary tract infection. False positive results have, however, been reported in proteinuria, asymptomatic bacteriuria, acute haemorrhagic cystitis, prostatitis, and cystitis.^{21 22} In acute pyelonephritis positive results may be found in 62-69% of cases.^{21 23 24} Our results of immunofluorescence of antibody coated bacteria in patients with acute pyelonephritis confirm the conclusion of Mundt and Polk that the test does not have a role in the management of patients with urinary tract infection because of its low sensitivity (83.1%) and specificity (76.7%).²⁶ Among the possible non-invasive techniques, scintiphotography with ^{67}Ga and determination of excretion of urinary β_2 microglobulin are currently the most appropriate for the diagnosis of renal inflammation. Moreover, serial determinations of urinary β_2 microglobulin excretion are useful in controlling the efficacy of treatment with antibiotics.

GHC was supported by a grant from the Netherlands Kidney Foundation. We thank M Ruijters for typing the manuscript.

References

- ¹ Anonymous. Bacteriuria—when does it matter? [Editorial]. *Lancet* 1979;ii:1166-7.
- ² Kass EH. The search for asymptomatic pyelonephritis. *N Engl J Med* 1972;287:563-4.
- ³ Davidson AJ, Tainer LB. Urographic and angiographic abnormalities in adult onset acute bacterial nephritis. *Radiology* 1973;106:249-56.
- ⁴ Cameron DD, Azimi F. The value of excretory urography in the diagnosis of acute pyelonephritis. *J Urol* 1974;112:546-9.
- ⁵ Silver TM, Kass EJ, Thornbury JR, Konnak JW, Wolfman MG. The radiological spectrum of acute pyelonephritis in adults and adolescents. *Radiology* 1976;118:65-71.
- ⁶ Kessler WO, Gittes RF, Hurwitz SR, Green J. Gallium-67 scans in the diagnosis of pyelonephritis. *West J Med* 1974;121:91-3.
- ⁷ Hurwitz SR, Kessler WO, Alazraki P, Ashburn WK. Gallium-67 imaging to localize urinary tract infections. *Br J Radiol* 1976;49:156-60.
- ⁸ Kumar B, Coleman RE. Significance of delayed 67-Ga localization in the kidneys. *J Nucl Med* 1976;17:872-5.
- ⁹ Mendez G Jr, Morillo G, Alonso M, Isikoff MB. Gallium 67 radionuclide imaging in acute pyelonephritis. *AJR* 1980;134:17-22.
- ¹⁰ Handmaker H. Nuclear renal imaging in pyelonephritis. *Semin Nucl Med* 1982;12:246-53.
- ¹¹ Schardin G, Statius van Eps LW, Swaak AJG, Kager JCGM, Persijn JP. Urinary β_2 -microglobulin in upper and lower urinary tract infections. *Lancet* 1979;ii:805-7.
- ¹² Tsan MF, Chen WY, Scheffel U, Wagner HN. Studies on gallium accumulation in inflammatory lesions: gallium uptake by human polymorphonuclear leukocytes. *J Nucl Med* 1978;19:36-43.
- ¹³ Hoffer PB, Huberty J, Khayam-Bashi H. The association of Ga-67 and lactoferrin. *J Nucl Med* 1977;18:713-7.
- ¹⁴ Menon S, Wagner HN, Tsan MF. Studies on gallium accumulation in inflammatory lesions. Uptake by *Staphylococcus aureus*. *J Nucl Med* 1978;19:44-7.
- ¹⁵ Tsan MF. Studies on gallium accumulation in inflammatory lesions. Roles of polymorphonuclear leukocytes and bacteria. *J Nucl Med* 1978;19:492-5.
- ¹⁶ Bekerman C, Vyas MI. Renal localization of gallium 67 citrate in renal amyloidosis. *J Nucl Med* 1976;17:899-901.
- ¹⁷ Myerson PJ, Myerson DA, Spencer RP, Prokop E. ⁶⁷Ga-citrate identification of inflammation in the perirenal space. *Clin Nucl Med* 1978;3:434-6.
- ¹⁸ Graham G, Lundy MM, Moreno AJ. Failure of gallium-67 scintigraphy to identify reliably noninfectious interstitial nephritis. *J Nucl Med* 1983;24:568-70.
- ¹⁹ Ormrod D, Miller T, Stewart E. Detection of renal infection by gallium-67 localization. An experimental evaluation. *Kidney Int* 1977;12:157-63.
- ²⁰ Biskjaer N, Thelle T. Pyelonefritiske parenchymdefekter hos børn bedømt ved ^{99m}Tc-DMSA nyrescintigrafi og iv urografi. *Ugeskr Laeger* 1983;145:1604-6.
- ²¹ Thomas V, Shelokov A, Forland M. Antibody-coated bacteria in the urine and the site of urinary-tract infection. *N Engl J Med* 1974;290:588-90.
- ²² Rumans LW, Vosti KL. The relationship of antibody coated bacteria to clinical syndromes. *Arch Int Med* 1978;138:1077-81.
- ²³ Thomas VL, Forland M. Antibody coated bacteria in urinary tract infections. *Kidney Int* 1982;21:1-7.
- ²⁴ Ratner JJ, Thomas VL, Sanford BA, Forland M. Bacteria-specific antibody in the urine of patients with acute pyelonephritis and cystitis. *J Infect Dis* 1981;143:404-12.
- ²⁵ Mundt KA, Polk BF. Identification of site of urinary tract infections by antibody coated bacteria assay. *Lancet* 1979;ii:1172-5.

(Accepted 2 May 1984)

SHORT REPORTS

Role of glucocorticoids in management of malignant hypercalcaemia

Glucocorticoids are commonly prescribed in malignant hypercalcaemia due to carcinoma¹ despite conflicting evidence on their efficacy.² We examined the effects of prednisolone on hypercalcaemia in patients with solid tumours.

Patients, methods, and results

We studied 28 patients with hypercalcaemia associated with solid tumours (breast, 17 patients; bronchus, six; cervix, four; hypernephroma, one). All but four patients had scintigraphic or radiographic evidence of metastases of bone. All patients were treated continuously with intravenous saline (4-6

portant component of management.⁵ As the efficacy of rehydration is commonly underestimated additional agents are often prescribed. Any hypocalcaemic response then observed may be due to the additional treatment rather than to rehydration. Our study suggests that the use of glucocorticoids to treat hypercalcaemia due to solid tumours is ineffective and that the responses observed were entirely attributable to rehydration. As steroids are not free of risk and have catabolic effects on bone we now avoid giving them to patients with malignant hypercalcaemia. Corticosteroids remain useful, however, in the treatment of hypercalcaemia due to other causes, particularly myeloma, sarcoidosis, and vitamin D toxicity.²

Mean (SEM) serum calcium and creatinine concentrations in patients with hyperglycaemia treated with rehydration alone or combined with corticosteroids

	Saline alone			Saline + steroids		
	Day 0	Day 3	Day 7	Day 0	Day 3	Day 7
Adjusted serum calcium (mmol/l)	3.49 (0.13)	3.21 (0.13)**	2.86 (0.16)*	3.56 (0.17)	3.24 (0.12)**	3.02 (0.08)**
Serum creatinine (μ mol/l)	0.119 (9.8)	108 (13.3)**	80 (10)*	148 (22)	131 (27)*	103 (13)**

Significance of changes induced by treatment: * $p < 0.02$; ** $p < 0.01$.

Conversion: SI to traditional units—Calcium: 1 mmol/l = 4 mg/100 ml. Creatinine: 1 μ mol/l $\approx$ 11.3 μ g/100 ml.

litres daily), and 15 were additionally treated with prednisolone (20-60 mg daily by mouth). None of the patients received diuretics, chemotherapy, or other agents likely to affect the serum calcium concentration. Venous blood samples obtained before treatment and at three and seven days were analysed for serum calcium, creatinine, and albumin concentrations with a Technicon SMAC AutoAnalyzer. Calcium values were adjusted to an albumin concentration of 42 g/l. The significance of changes between mean values was assessed with a two tailed Wilcoxon's rank sum test for paired observations. Results are expressed as means (SEM).

Patients given saline alone and those given saline and prednisolone were similar with regard to age (64 (3) v 51 (3) years); initial serum calcium concentration (3.49 (0.13) v 3.56 (0.17) mmol/l (14 (0.5) v 14 (0.7) mg/100 ml)); serum albumin concentration (35 (1) v 35 (1) g/l); and serum creatinine concentration (119 (10) v 131 (27) μ mol/l (1.3 (1.1) v 1.5 (0.3) mg/100 ml)). Treatment with saline alone induced a significant fall in serum calcium concentrations (mean decrease 0.40 (0.12) mmol/l (1.6 (0.5) mg/100 ml) at seven days), which was associated with a significant fall in serum albumin and creatinine concentrations (table). The addition of prednisolone to the intravenous fluid regimen did not confer any additional benefit.

Comment

Dehydration helps to perpetuate or aggravate hypercalcaemia of whatever origin,^{3 4} and, therefore, attention to fluid balance is an im-

portant component of management.⁵ As the efficacy of rehydration is commonly underestimated additional agents are often prescribed. Any hypocalcaemic response then observed may be due to the additional treatment rather than to rehydration. Our study suggests that the use of glucocorticoids to treat hypercalcaemia due to solid tumours is ineffective and that the responses observed were entirely attributable to rehydration. As steroids are not free of risk and have catabolic effects on bone we now avoid giving them to patients with malignant hypercalcaemia. Corticosteroids remain useful, however, in the treatment of hypercalcaemia due to other causes, particularly myeloma, sarcoidosis, and vitamin D toxicity.²

(Accepted 8 May 1984)

Department of Human Metabolism and Clinical Biochemistry, University of Sheffield Medical School, Sheffield S10 2RX

RICHARD C PERCIVAL, FRCS, Wellcome surgical research fellow
ASHLEY J P YATES, MRCP, Medical Research Council clinical research fellow

RICHARD E S GRAY, MA, MRCP, research fellow
FRANK E NEAL, FRCP, consultant radiotherapist and oncologist
A ROBERT W FORREST, MRCPATH, consultant chemical pathologist
JOHN A KANIS, MRCP, reader

Correspondence to: Dr J A Kanis.