A number of mechanisms have been shown to underlie the pathogenesis of angiotensin II effects on the transglomerular passage of protein. These include modulation of efferent arteriolar tone, intraglomerular pressure and glomerular plasma flow as well as changes in the ultrafiltration co-efficient and size-dependent barrier functions [9,10]. Whilst abrogation of the loss of nephrin expression by RAS blockade has been demonstrated in the long-term injury of acquired proteinuric renal disease, it is unknown whether this represents a direct effect of angiotensin II on the podocyte or a secondary effect in preserving the structural integrity of the glomerulus. Indeed, our group has recently shown that in diabetes, the long-term structural changes, rather than short-term effects of hyperglycaemia were associated with the reduction in nephrin in that disease [7].

The findings of the present study suggest that despite increased expression of nephrin with blockade of the RAS [4,7,11,12], angiotensin II does not directly decrease nephrin expression. Indeed, rather than the expected decrease in nephrin mRNA with angiotensin II, the present study, using two different methods of assessment, documented an ~2-fold increase in gene expression in response to continuous infusion. The mechanisms whereby angiotensin II leads to increased nephrin expression are unknown. However, angiotensin II is a potent activator of protein kinase C [13], a key intracellular signalling system in the regulation of nephrin expression [14].

We therefore suggest that the previously documented effects of ACE inhibition and ARBs reflect the actions of these agents in preserving renal structure and function, rather than a direct effect of RAS blockade on podocyte nephrin transcription. We further suggest caution in interpreting the findings of studies reporting modulation of nephrin expression in acquired renal disease and the effects of therapeutic intervention.

Acknowledgements. This work was supported in part by grants from the National Health and Medical Research Council of Australia and the Juvenile Diabetes Research Foundation International. Darren J. Kelly is a recipient of a career development award from Juvenile Diabetes Research Foundation. The authors are indebted to Mariana Pacheco for her excellent technical assistance.

Conflict of interest statement. None declared.

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DOI: 10.1093/ndt/gfg509

Pseudoephedrine urolithiasis associated with acute renal failure

Sir,

A 20-year-old male was taking ibuprofen for back pain and developed nausea, vomiting and peripheral oedema. His creatinine was 7.9 mg%. Renal ultrasound showed bilateral hydropneumosisis. Ureteral stents were placed for probable papillary necrosis from ibuprofen and his creatinine fell to 1.1 mg%. Three months later his creatinine was 1.7 mg%. Renal ultrasound again showed hydropneumosisis and an echogenic focus with shadowing. Plain X-rays of the abdomen were negative. Bladder calculi were found on cystoscopy and retrograde studies showed filling defects in the pelvis of the kidney. Recovered stone material was analysed and revealed 92% (Pseudo)ephedrine, 3% calcium phosphate and 5% protein. He had been taking pseudoephedrine for sinus headaches since age 9 years. Over the past 2 years he had increased the dose to 10, 60 mg tablets per day.

A 24-h urine sample was collected when his renal function was normal. His urine volume was 1125 ml/day. Urinary
calcium excretion was 407 mg/day (NL < 300 mg/day), oxalate 18 mg/day (NL < 45 mg/day) and citrate 0.127 mmol/day (NL 1.861–4.303 mmol/day). He failed further follow-up.

This patient presented with acute renal failure from obstructive uropathy associated with radiolucent material composed of pseudoephedrine. Drug-induced urolithiasis is not uncommon [1] and there are previous reports of ephedrine containing renal stones usually accompanied by quaiifenesin [2–5].

The 24-h urine collection revealed a low urine volume, hypercalciuria and hypocitraturia. Low urine volume is a recognized risk factor for all types of stone. Hypercalciuria is a risk factor for calcium stone disease and this patient had calcium phosphate as a part of his stones. However, the calcium phosphate was present in the intercystalline voids suggesting it did not initiate stone formation but had precipitated on the pseudoephedrine. Hypocitraturia has been reported previously in patients with guaiifenesin/ephedrine stones but the cause has not been investigated [4]. The patient failed to follow up before the hypocitraturia could be evaluated.

These stones can be added to the list of radiolucent stones and can be added to the growing list of drug-induced stones. It is characterized by frequent recurrence and may be associated with hypocitraturia. This type of stone disease will prove difficult to treat as it likely represents addiction to these stimulant drugs.

Conflict of interest statement. None declared.

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DOI: 10.1093/ndt/gfg510