ischaemia-reperfusion, plasma creatinine concentrations were significantly lower in thiamine-deficient rats than in control rats (71.7 ± 22.2 versus 162 ± 106, respectively, $P = 0.02$).

In this study, we found that thiamine deficiency complicated by weight loss is protective against renal IRI rather than a factor that increases susceptibility. Interestingly, it is long known that in hearts prolonged fasting protects against IRI [7]. To the best of our knowledge our study is the first to suggest that a similar phenomenon may be present for the kidney. If future studies confirm that fasting/wasting protects against IRI in the kidney, this may lead to identification of new mechanisms and methods for priming of kidneys for prevention of IRI.

Conflict of interest statement. None declared.

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1. Perico N, Cattaneo D, Sayegh MH *et al*. Delayed graft function in kidney transplantation. *Lancet* 2004; 364: 1814–1827
2. Larrieu AJ, Yazdanfar S, Redovan E *et al*. Beneficial effects of cocarboxylase in the treatment of experimental myocardial infarction in dogs. *Am Surg* 1987; 53: 721–725
3. Sheline CT, Wei L. Free radical-mediated neurotoxicity may be caused by inhibition of mitochondrial dehydrogenases in vitro and in vivo. *Neuroscience* 2006; 140: 235–246
4. Klooster A, Leuvenink HG, Gans RO *et al*. Tissue thiamine deficiency as potential cause of delayed graft function after kidney transplantation: thiamine supplementation of kidney donors may improve transplantation outcome. *Med Hypotheses* 2007; 69: 873–878
5. Chamberlain BR, Buttery JE, Pannall PR. A stable reagent mixture for the whole blood transketolase assay. *Ann Clin Biochem* 1996; 33(Pt 4): 352–354
6. Lynch PL, Young IS. Determination of thiamine by high-performance liquid chromatography. *J Chromatogr A* 2000; 881: 267–284
7. Schaefer S, Ramasamy R. Glycogen utilization and ischemic injury in the isolated rat heart. *Cardiovasc Res* 1997; 35: 90–98

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RET gene mutations are not a common cause of congenital solitary functioning kidney in adults

Sir,

RET (rearranged during transfection) is a transmembrane receptor tyrosine kinase. Loss-of-function *RET* mutations occur in Hirschsprung disease, while gain-of-function mutations cause multiple endocrine neoplasia type 2 (MEN2) and familial medullary thyroid carcinoma (FMTC) [1]. In mice, Ret initiates mouse kidney development by enhancing ureteric bud outgrowth [2]. Renal agenesis occurs in mice with homozygous null mutation of either *Ret*, *Gdnf* or *Gfra1*, the latter two genes, respectively, coding for a key ligand that activates Ret and a Ret co-receptor [2].

In humans, unilateral renal agenesis occurs in around 0.01% births and results in a solitary functioning kidney, whereas bilateral renal agenesis and/or severe dysplasia occurs in a similar frequency and usually leads to neonatal death [3].

A role for RET in human kidney development was suggested by a report of unilateral renal agenesis in two members of a FMTC family with *RET* mutation [4]. More recently, *RET* mutations were reported in 7 of 19 fetuses with bilateral renal agenesis, and in 2 of 10 with unilateral agenesis and contralateral dysplasia [5]. However, the prevalence of *RET* mutations in adults with congenital solitary functioning kidney is unknown.

A cohort of 14 subjects were selected for our current study. They were living adults born with a solitary functioning kidney, one of whom had two failed pregnancies with fetuses affected by malformed kidneys. We screened exons 1–20 and the conserved splice-sites of *RET* using direct sequencing. None of the cohort were known to have Hirschsprung disease or MEN2/FMTC or other recognized genetic syndrome. We did not identify any mutations in the 14 adults, and thus it is unlikely that *RET* mutations will be a common cause of solitary functioning kidney in adults.

Because mutations of *hepatocyte nuclear factor 1B* have been reported in the context of solitary functioning kidney [6], we also screened this gene by sequencing and by dosage analysis but failed to find mutations. Other genes such as *GDNF* and *GFRA1* have yet to be elucidated in our cohort.

Our study was in adults while Skinner *et al*. [5] studied fetuses. We therefore suggest that human *RET* mutations causing renal disease lead to severe renal failure incompatible with postnatal survival. Mutations of nephrogenesis genes other than *RET* should be sought to explain human congenital solitary functioning kidney.

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1. Runeberg-Roos P, Saarma M. Neurotrophic factor receptor RET: structure, cell biology, and inherited diseases. *Ann Med* 2007; 39: 572–80
2. Costantini F, Shakya R. GDNF/Ret signaling and the development of the kidney. *Bioessays* 2006; 28: 117–127
3. Wiesel A, Queisser-Luft A, Clementi M *et al*. EUROSCAN Study Group. Prenatal detection of congenital renal malformations by fetal ultrasonographic examination: an analysis of 709,030 births in 12 European countries. *Eur J Med Genet* 2005; 48: 131–144
4. Lore F, Di Cairano G, Talidis F. Unilateral renal agenesis in a family with medullary thyroid carcinoma. *N Engl J Med* 2000; 342: 1218–1219
5. Skinner MA, Safford SD, Reeves JG *et al*. Renal aplasia in humans is associated with RET mutations. *Am J Hum Genet* 2008; 82: 344–351
6. Bingham C, Ellard S, Cole TRP *et al*. Solitary functioning kidney and diverse genital tract malformations associated with hepatocyte nuclear factor-1 mutations. *Kidney Int* 2002; 61: 1243–1251

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An unconscious 76-year-old woman with renal failure and hyperechoic kidney lesions

Sir,

Overall rates of infection with *Mycobacterium tuberculosis* have declined over recent years in most western countries. However, tuberculosis remains a problem in certain high-risk groups [1,2]. Postprimary tuberculosis is even rarer, especially causing chronic renal failure [3]. Thus, attention to this (once) common disease is most likely low in the present generations of physicians in industrialized countries.

The present case shows that a careful workup of renal insufficiency, particularly considering anamnesis and clinic, can still lead to an unexpected diagnosis. This case report should encourage clinicians to consider tuberculosis in differential diagnosis, especially in the patient at risk.

A 76-year-old white, cachectic female was admitted to the university hospital as an emergency case. On presentation at the emergency department in June 2008, she had a Glasgow coma scale of 5 and a body temperature of 36°C. The respiratory rate was increased despite normal O_2 saturation. Tachycardia and arterial hypertension were detected. Physical examination showed a pale, dehydrated and cachectic woman (BMI 13.3) with normal auscultation of the lung, normal physical abdominal findings, absence of skin abnormalities and meningism, and without focal neurological signs. A CT scan excluding bleeding and raised intracranial pressure was performed. The patient was transferred to a neurological intensive care unit where she underwent lumbar puncture. Cerebrospinal fluid cell count, protein concentration and gram staining were normal. Blood analysis revealed Na^+ 138 mmol/L, K^+ 5.9 mmol/L, Ca^{2+} 2.5 mmol/L (corrected for serum albumin), serum–creatinine 203 μmol/L, blood urea nitrogen 14.6 mmol/L, haemoglobin 75 g/L, prolactin 1000 pmol and CRP 18 mg/L. Although her medication included carbamazepine, it was not traceable in blood analysis on the day of presentation.

Sixteen months previously, our patient had been admitted to the department of neurosurgery in a community hospital due to persistent headache and vomiting. Hypertrophic pachymeningitis was confirmed histologically. After the neurosurgical procedure, the patient suffered from symptomatic epilepsy. For this reason, she was admitted twice at different hospitals (March and April 2008) and treatment with carbamazepine (400 mg bid) was commenced. Serum–creatinine was elevated (177 μmol/L) on both occasions despite a normal creatinine 1 year before. The patient's past medical history also revealed the development of arterial hypertension, anaemia and severe weight loss within the previous year.

Treatment in the department of neurology consisted of rehydration, blood transfusion and carbamazepine saturation. Due to increased serum creatinine, the consultant nephrologist was involved. At presentation, diuresis was 950 mL/day and GFR was 13 mL/min. Urinalysis was negative except for traces of protein. Differentiation of the mild proteinuria revealed moderate elevated albumin, IgG and alpha-1-microglobuline. The urine culture was negative. B-mode kidney ultrasound showed a left kidney of 10.8 × 4.3 cm and a right kidney of 8.5 × 2.2 cm. Both kidneys presented with multiple, disseminated nodulous (2–4 mm) hyperechoic lesions of the parenchyma. There were no hints towards kidney stones or postrenal obstruction. Perfusion was adequate. Mycobacteria were not detected in the urine (PCR and culture). Abnormal ultrasonography qualified the patient for a kidney core needle biopsy. Histology showed the presence of necrosis with focal epithelioid cells as a central proportion of granuloma (caseous lesions, indicative for tuberculosis) whereas interstitial fibrosis was absent (Figure 1). Chest CT scan was not probative for active tuberculosis, yet typical older lesions were seen [4]. Anti-tuberculous therapy was commenced immediately [quadruple regimen with ethambutol 500 mg (tid), isoniazid/vitamin B6 200 mg/day, rifampicin 300 mg/day and pyrazinamide 1500 mg/day)].

The patient stabilized and was discharged into a nursing home, with daily medication consisting of carbamazepine 600 mg (bid), amlodipin, lisinopril, hydrochlorthiazide, torasemide, calcitriol and darbepoetin-alpha 30 μg sc (weekly).

Four months after the initiation of tuberculostatic therapy, she has gained 4 kg of body weight, her well-being improved constantly and kidney function has recovered to 24.2 mL/min (MDRD GFR).

Extrapulmonary tuberculosis affecting the genitourinary system is usually caused by haematogenous dissemination of *M. tuberculosis* from the lungs (reasonably responsible for the renal tuberculosis of our patient). However, <50% of these patients give radiographical evidence for pulmonary tuberculosis, whereas active disease is present in only 5% of such patients [5]. Presumably 10% of all patients with tuberculosis develop reactivation. Their risk is highest within the first 2 years or during periods of immunosuppression [2]. Indeed our patient showed pulmonary radiographical findings consistent with older tuberculous lesions. Notably, even in high-risk patients with a history of tuberculosis who received a renal transplant postprimary renal tuberculosis is rare [6]. In a recent report on 80 patients with