commonly associated with confusion in the elderly. Either of these factors are plausible explanations for the confusion experienced by this patient.

In summary, this patient with known diverticular disease presented with a febrile episode that responded to antibiotic treatment. The authors noted the expected radio-opaque appearance of lanthanum in the gastrointestinal tract and plasma lanthanum levels within the range observed in pivotal clinical trials. Neither finding has been convincingly linked to the patient's presentation; therefore, there are no grounds for revising the benefit–risk profile for LC.

Conflict of interest statement. MS and RDP are employees of Shire Pharmaceuticals.

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Reply

In response to Dr Smyth's letter to the editor, we would like to remind readers that lanthanum carbonate has indeed shown its efficacy, but that many safety concerns remain unsolved. We would like to draw attention to two main points brought out in our case report:

1. Gastro-intestinal effects: Lanthanum has been shown to induce a number of gastrointestinal effects [1].

Patients with acute peptic ulcer, ulcerative colitis, Crohn disease or bowel obstruction were not included in the pivotal FOSRENOL(R) study, its 6-year follow-up report [2] or in Finn's work [3]. Therefore, caution should be exercised in patients with these conditions [4]. There was more withdrawal in patients treated with lanthanum mainly attributable to digestive disorders in these studies. Our patient had previous digestive disorders and therefore should be considered a high-risk patient for digestive side effects.

In our patient, the plasmatic lanthanum level was 2.13 μg/l. In the public assessment report [5], the mean concentration for long-term ingestion of 3 g lanthanum/day ranges from 0.5 to 0.6 ng/ml. There was no significant dose or time effect on treatment. Altman's study reported the same mean plasmatic value—0.3 ng/ml—but a wide range (0.0–3.1 ng/ml). More information would be required to explain this difference.

It has been shown that the tissue concentration is higher than the plasma concentration so we cannot assume that lanthanum is not nontoxic. Tissue accumulation is seen particularly in the gastro-intestinal tract, lymphoreticular system, bone, liver and spleen [5]. Recently, Davis and Jerrold reported the detection of lanthanum deposits in a mesenteric lymph node in a patient 3 years after exposure [6].

The degree of digestive absorption has not been evaluated, nor has the excretion of the unabsorbed dose of lanthanum in the faeces been demonstrated in humans [5,7].

The two FDA reviewers for market approval of lanthanum (Drs Pelayo and Oluferni [1]) made a negative recommendation because of the gastro-intestinal effects and the unknown accumulation and elimination of the product, which presented 'a real risk of malnutrition and additional injury in this population'. They stated that it can be 'unacceptably toxic'. The sponsor was in charge of providing proof on this point but was unable to do so.

2. The effects on the central nervous system: a number of animal studies indicate significant brain exposure [8].

The blood–brain barrier can be damaged when there is significant inflammation, tumours, etc. and can allow selective delivery of pharmacological agents to the brain [9]. The impact of lanthanide on brain function is not insignificant [10]. It is known that when it passes the blood–brain barrier in animals, it can be toxic to the nervous system and cognition [11,12]. In healthy rats, Damment *et al*. [13] showed that the lanthanum brain concentration found is considered contamination.

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There is insufficient evidence to conclude that lanthanum cannot cross the blood–brain barrier in healthy or uraemic patients, not to mention infected haemodialysed patients.

Many publications agree that further investigation and more time are needed before it can be firmly concluded that the tissue accumulation is nontoxic, with no severe adverse effects [14].

The Transparency Committee of the French National Authority for Health (Haute Autorité de Santé) has stated that safe long-term use of lanthanum is not established given that it accumulates in bone, brain and heart.

We fully agree with Smith and Pratt that the benefice-risk ratio need not to be revised based on our case report alone. However the nephrological community needs to be reminded that a product's safety, especially in dialysis patients, is the cornerstone of patient care. We merely emphasize that this medication should not be used in the case of inflammatory or gastro-intestinal disorders since none of the studies conducted to date have included patients with these pathologies [1–3]. In addition, the product label clearly states that the product should not be administered to these patients [5,15]. Our article is a reminder that prescription of this medication is restricted and a warning that previously reported adverse effects may occur.

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Letter

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Prescribing peritoneal dialysis in each patient with uremic toxins as the treatment marker

Sir,

Vilar demonstrated that residual renal function (RPF) is important not only in PD, but also in HD. All these benefits occur despite those with RRF having a lower delivered HD dose [1].

We examined the number of PD bag exchanges in 79 incident PD patients with RPF at our hospital from January 2006 to June 2009. The result was that one bag (2 L) was exchanged in 2% of the patients, two bags in 44%, three bags in 46% and four bags in 8%. We increased the number of bag exchanges in patients who had uncontrolled fluid accumulation and poor solute removal (e.g., β_2-microglobulin (β_2 MG)>35 pg/ml) or EPO-resistant anaemia. Among the 37 incident PD patients in whom one to two bags were exchanged, 1 died and 2 received renal transplants. Of the 28 patients who continued PD for more than 1 year, 19 (68%) received continuous PD treatment with exchange of one to two bags (Figure 1). In these patients, RPF maintained, although urine volume decreased from 1440 ± 364ml/day to 1020 ± 589 ml/day slightly during 1 year.

At the end of 2006, nearly 320 000 ESRD patients were receiving haemodialysis therapy, 25 438 were being treated with peritoneal dialysis (PD) in the United States and they are rapidly aging. We should consider medical costs and QOL when performing PD treatment. Increasing the PD solution volume was recommended in the NKF-K/DOQI and other guidelines before 2000, because these were believed to improve the prognosis. However, Lo et al. reported that it is not solution volume but residual renal function that affects the prognosis [2]. Therefore, performing PD with a similar solution volume in all patients is not rational, so we investigated low-volume PD in this study.

The solution volume used to be considered to be important in PD treatment, but it seems that we should change the therapeutic strategy to target accumulation of uraemic toxins such as β_2 MG and control accumulation of fluid, which have also been shown to be associated with the prognosis in patients on HD. We reported that accumulation of uraemic toxins such as β_2 MG leads to peritoneal injury or EPS [3]. It is likely that prescribing PD in each patient with uraemic toxins as the treatment marker will contribute to reducing medical costs and improving the QOL.