Phosphate retention occurs as patients develop progressive chronic kidney disease, and healthy patients achieving recommended nutritional targets typically require oral phosphate binders to limit phosphate absorption [1]. We were prompted to measure trace elements following a case of severe copper deficiency in a patient following gastric bypass surgery for morbid obesity [2], and in vitro studies have suggested that ion-exchange resins, including sevelamer, can potentially bind trace metals, including copper and zinc. Although some patients had trace element levels below the normal reference, this did not appear to be associated with phosphate binder prescription [3], but rather to dietary intake and recent or concurrent illnesses. Although the dialysis prescription [4] and modality [5] have been reported to impact on serum calcium and phosphate, the data to date do not suggest any significant clearance of water-soluble vitamins by different dialysis modalities, provided that patients have an adequate diet [6]. However, Schiff and Lang have now questioned whether the prescription of the ion-exchange phosphate binder, sevelamer hydrochloride, can bind water-soluble vitamins, so reducing gastrointestinal absorption and resulting in clinically apparent vitamin deficiency.

Conflict of interest statement. None declared.

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Varicella-zoster virus meningoencephalitis without skin lesions in a paediatric kidney recipient

Sir,

We have read with great interest the exceptional case reported by Jantsch et al. concerning a case of lethal varicella-zoster virus (VZV) reactivation without skin lesions following renal transplantation [1]. Recently, we treated an 11-year-old girl for VZV meningoencephalitis without skin lesions.

At age 5, she was diagnosed with nephrotic syndrome related to diffuse mesangial sclerosis. Despite immunosuppressive therapy with steroids and oral cyclosporine, end-stage renal disease occurred within 6 months. At age 7, after an 8-month haemodialysis period, she received a kidney transplant. Maintenance immunosuppression consisted of mycophenolate mofetil, tacrolimus and low-dose steroids on alternate days.

Despite a typical VZV eruption occurring at age 3, the patient was negative for VZV IgG and IgM before transplantation. VZV vaccination was not performed during the haemodialysis period. Three years after renal transplantation, she developed a typical VZV eruption without organ involvement. She was successfully treated with oral valacyclovir.

Four years after renal transplantation, at age 11, she was referred to our unit for febrile somnolence. On physical examination, meningoencephalitis was present, and Glasgow score was 10. There was no other physical sign and especially no skin lesions. Cerebral CT scan was normal. Spinal fluid examination displayed hypercellularity (90 cells/mm3; 93% of lymphocytes) with elevated protein concentration (0.99 g/L) and normal level of glucose. Bacterial and fungal cultures and testing for toxoplasmosis and *Cryptococcus* infection were negative. Viral DNA analysis was negative for herpes simplex viruses 1 and 2, enterovirus, cytomegalovirus, Epstein–Barr virus, and human herpes virus 6, but positive for VZV. Serum VZV IgG and IgM were both negative. Electroencephalogram displayed typical features of encephalitis. Diagnosis of VZV meningoencephalitis was considered, and intravenous (IV) acyclovir (500 mg/m² TID) was started. She also received two doses of specific anti-VZV human antibodies (Varitect®). Her condition improved within 3 days, and acyclovir was stopped after 10 days. On discharge, physical examination was normal.

In paediatric kidney recipients, VZV reactivation is a rare feature, mostly described in the first year after transplantation [2]. Our report is the first case of VZV meningoencephalitis without skin lesions in a paediatric kidney recipient.
recipient. VZV meningoencephalitis has until now only been described after bone marrow transplantation [3]. As discussed by Jantsch et al., this report emphasizes the importance of systematic assaying for VZV IgG and IgM before transplantation, irrespective of past history of VZV eruption. VZV vaccination should be proposed before renal transplantation in seronegative patients. It has been demonstrated to be immunogenic and safe in paediatric patients with chronic kidney disease [4]. Up to now, there are not enough data to propose systematic VZV vaccination after renal transplantation in seronegative recipients.

Conflict of interest statement. None declared.

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doi: 10.1093/ndt/gfq636

Advance Access publication 8 October 2010

Reply

Sir,

With interest, we read the case report and comments by Garnier et al. concerning our recently published manuscript on a lethal varicella-zoster virus (VZV) reactivation without skin lesion following renal transplantation (RTX). The report by Garnier et al. raises two questions: (i) What is the best method to assess VZV-specific immunity? (ii) What is the optimal regimen for prophylaxis of VZV reactivation?

First of all, it is important to emphasize that the two cases differ substantially. While our case describes a lethal VZV reactivation of a ‘68-year-old’ woman after RTX who has been ‘seropositive’ for VZV IgG prior to transplantation [1], Garnier et al. reported on a ‘11-year-old’ girl who suffered from VZV meningoencephalitis after RTX who had been ‘seronegative’ for VZV IgG and IgM prior to transplantation despite a documented VZV infection at the age of 3.

In elderly patients, the frequency of anti-VZV T cells rather than VZV-specific Ig titres correlates with control of VZV [2]. Therefore, positive VZV-specific Ig titres alone do not allow to assume VZV-specific immunity as our case clearly demonstrates [1]. We propose to carry out prospective studies on the quantitation of VZV-specific T cells in VZV-seropositive as well as VZV-seronegative patients as a future basis for a reliable assessment of the risk of VZV reactivation after RTX.

Since there are studies demonstrating that the loss of VZV-specific antibodies increases the likelihood for VZV disease [3], we agree with Garnier et al. that vaccination prior to RTX should be considered in VZV-seronegative patients. However, the situation may be different in elderly, VZV-seropositive patients with chronic kidney disease, who have been on dialysis treatment for several years and are awaiting renal transplantation. As outlined in our case report, several lines of evidence question whether the immune system of these patients is able to mount a protective VZV-specific immune response [1]. Thus, vaccination against VZV prior to RTX may not sufficiently boost cellular immunity in all cases. In summary, further studies are needed to determine precisely the risk factors and risk-stratified treatment options for adult and paediatric patients awaiting RTX.

Conflict of interest statement. None declared.

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doi: 10.1093/ndt/gfq637