has been discussed to cause suppression of cellular immunity [4]. However, our patient with long-standing RA was treated with MTX, LEF and low-dose prednisolone for 4 yrs without any major complications but contracted Pneumocystis pneumonia 4 months after LEF was stopped and rituximab was administered. The strong temporal relationship between the rituximab infusions and the onset of the disease suggests that rituximab played a decisive role in the development of the opportunistic infection.

The host’s defence against Pneumocystis is thought to be critically dependent on the activity of CD4+ T cells. There is growing evidence supporting the notion that rituximab not only depletes B cells but also influences T-cell immunity. Remarkably, the occurrence of infectious diseases generally considered to be associated with T-cell immunosuppression has been reported after rituximab administration. On 18 December 2006, the US Food and Drug Administration (FDA) issued a safety information warning that two patients receiving rituximab for the treatment of SLE had developed progressive multi-focal leucoencephalopathy caused by reactivated JC virus [5]. Furthermore, there are 15 published cases of CMV infections after rituximab administration [6]. In context with our case, we wish to highlight a recent publication [7] reporting six cases of Pneumocystis pneumonia in a group of 46 B-cell lymphoma patients treated with the rituximab-CHOEP-14 regimen [Cyclophosphamide 750 mg/m² IV on day 1, Doxorubicin 50 mg/m² IV on day 1, Vincristine 1.4 mg/m² (max 2 mg) on day 1, Etoposide 100 mg/m² IV day 1 to day 3, Prednisolone 100 mg PO on days 1-5; Repeat cycle every 4 weeks] [6]. In context with our case, we wish to highlight a recent publication [7] reporting six cases of Pneumocystis pneumonia in a group of 46 B-cell lymphoma patients treated with the rituximab-CHOEP-14 regimen [Cyclophosphamide 750 mg/m² IV on day 1, Doxorubicin 50 mg/m² IV on day 1, Vincristine 1.4 mg/m² (max 2 mg) on day 1, Etoposide 100 mg/m² IV day 1 to day 3, Prednisolone 100 mg PO on days 1-5; Repeat cycle every 15 days], compared with one out of 25 patients in the CHOEP-14 group without rituximab (13% vs 4%).

The underlying mechanisms involved in the aforementioned clinical observations are ill defined. Interestingly, B-cell deficient mice fail to clear Pneumocystis infection probably due to inefficient generation of protective CD4+ memory and effector T cells [8]. Sfikakis and colleagues [9] reported that clinical remission of lupus nephritis following B-cell depletion with rituximab is associated with a decrease in T helper cell activation. Moreover, mRNA levels of the regulatory T-cell marker FoxP3 in peripheral blood lymphocytes increased significantly in patients with lupus nephritis after rituximab therapy [10]. Whether rituximab modulates T-cell immunity and predisposes to Pneumocystis pneumonia remains to be clarified.

**Rheumatology key message**

- Rituximab might modulate T-cell immunity.

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5 US Food and Drug Administration. FDA alert: rituxan (marketed as Rituxan), December 2006.


**Inflammatory aortitis controlled by the Chinese herbal remedy Donglingcao Pian**

**SIR,**

GCA is a systemic vasculitis common in elderly patients. It most commonly affects extracranial branches of the carotid arteries such as the temporal arteries but also less commonly large vessels such as aorta and medium vessels such as coronary arteries.

In many cases, the diagnosis of GCA is straightforward. Patients typically present with unilateral headache, and have temporal artery tenderness on examination. The investigations show elevated inflammatory markers and biopsies of the temporal arteries may show typical inflammatory changes. Some patients may have classical PMR symptoms as there is an overlap between these two conditions [1]. A small proportion of patients can have clinically ‘silent’ GCA and may present as pyrexia of unknown origin or other systemic features such as weight loss or night sweats. In such cases, the diagnosis can be delayed.

Our patient had been well until 1992 when at the age of 54, following a viral illness, she developed chronic fatigue syndrome. Her symptoms changed in 2002 with fatigue, chest discomfort, dyspnoea and a feeling of pressure in her head but no temporal headache. She had lost 2 stone in weight over a few months, and complained of intermittent fevers and night sweats. She was admitted for investigations at this time. General examination was unremarkable. In particular, all peripheral pulses were palpable and equal. There were no bruits detected. She had documented spikes in temperature. Investigations revealed a normocytic, normochromic anaemia of 10.1 g/dl, an elevated ESR at 102 mm/h and a CRP of 102 mg/l. Renal, liver and thyroid function tests were normal as were all tumour markers, ANA, ANCA and a serological screen (including hepatitis, HIV, TB and Legionella).

A chest X-ray, CT of her abdomen and pelvis, and a bone marrow biopsy were also normal. A PET scan showed increased uptake in the thoracic aorta and the great vessels suggestive of large-vessel vasculitis (Fig. 1a) (2003).

She was referred to the rheumatology department with a diagnosis of GCA, and was treated with pulse intravenous methylprednisolone followed by high-dose oral steroids that were gradually reduced. All blood indices normalized and she felt well.

By spring 2005 she was on oral prednisolone 2.5 mg daily. It was noted that her inflammatory markers were rising with each step reduction in prednisolone to a peak CRP of 12 over the...
In conclusion, we describe a patient with an inflammatory aortitis controlled with a Chinese herbal remedy with possible anti-TNF-α properties. There may be many potential new drugs to be found by investigating traditional herbal remedies that have been used for hundreds of years. However, unregulated use of some herbal remedies also has the potential of causing harm and even death.

**Rheumatology key message**

- Herbal remedies may have a place in the treatment of some chronic inflammatory conditions but more research is required.

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8 Hing Kwok Chu J. Donglincao, Rhabdosime rubescentis. Complementary and Alternative Healing University.
SIR, We read with interest the paper by Karie et al. on the MATRIX study and implication on RA-related drugs management: Comment on: Kidney disease in RA patients: prevalence and implication on RA-related drugs management: the MATRIX study.

We wish to highlight an issue regarding MTX prescribing and toxicity in chronic kidney disease (CKD) in patients with RA and report a case that has changed clinical practice in our unit [2].

A 77-yr-old female with a 40-yr history of RA, was stable on MTX therapy (original dose 15 mg once weekly). Following a gradual rise in serum creatinine (up to 170 µmol/l) MTX was stopped. It was later restarted at lower dose at the patient’s request (following a consultant renal physician opinion and investigations into the cause of the renal impairment). Her disease was then well controlled on a low dose of MTX 10 mg once a week. Other disease-modifying drugs (DMARDs) were considered but had failed in past. At the MTX restart her estimated glomerular filtration rate (eGFR) was calculated by the Cockcroft-Gault formula to be 24 ml/min (Stage 4 CKD, creatinine 200 µmol/l). The patient went on to regular blood monitoring over the next 15 months on 10 mg MTX once weekly with a normal full blood count and stable renal function.

She was admitted with non-specific malaise having had diarrhoea ~2 weeks earlier. Parameters recorded 16 days prior to her admission revealed a normal full blood count (white blood cell, differential platelet count) and static renal function. Her admission blood tests revealed a pancytopaenia, with an admission creatinine of 196 µmol/l. There had been no dosing error (tablet count), no new concomitantly prescribed medications and the tablet strength was checked by the hospital pharmacy. Bone marrow biopsy showed evidence of bone marrow failure with no other specific diagnostic features.

Despite intravenous folinic acid, anti-microbial treatment and multi-organ support in our Critical Care unit she died 7 days into her admission. Post-mortem showed no other major abnormalities and cause of death was reported as MTX toxicity.

Although there is limited published data on MTX clearance in CKD, trial data suggests that with an eGFR of <45 ml/min the expected 8 h level for a 10 mg dose is 0.11 µmol/l, with a half-life (1/2) of 22 h [3]. On admission, the free MTX level (30 h post dose) was 0.13 µmol/l. We presume that the episode of diarrhoea and vomiting prior to her admission had resulted in dehydration with a subsequent drop in renal clearance of MTX, leading to MTX/metabolite accumulation and subsequent toxicity.

This case highlights the dangers of MTX in CKD, even at reduced dose, and what can be falsely reassuring blood monitoring leading up to an adverse event. Following on from this experience we have instigated a number of changes to our clinical practice.

First, we now give written advice to all patients on MTX who have a significant inter-current illness, particularly those with CKD, to omit MTX until a full recovery has ensued. This will hopefully reduce accumulation of MTX and toxicity.

Second, we have arranged for the EGFR [calculated by the abbreviated Modification of Diet in Renal Disease Study (MDRD) equation as recommended by the UK Chronic Kidney Disease Guidelines] to be added to our computerized DMARD blood monitoring system. We are also asking for routine EGFR measurements on all our patients on blood monitoring for MTX.

Finally, we have reviewed our computerized monitoring system to identify all patients on MTX who have reduced eGFR and we are currently undertaking a case note review. To date, we have identified 18 patients with CKD Stage 4 (of 879 patients on MTX) under follow-up in our unit, on a reduced dose of MTX (the age range is 61–77, prevalence 2%). This is significant as Karie et al. describe no patients with CKD Stage 4 in their study. We suspect MTX is being used more commonly in an increasing elderly group of patients with added comorbidities.

The Renal Association provide both an online calculator for EGFR and have produced helpful online (and downloadable) EGFR tables that are practical and easily used by both Specialist Nurses and Rheumatologists in satellite clinics, etc [4]. This information can be used to make judgements on MTX dosage. There are a number of conflicting sources of advice for MTX dosing in CKD and there is a need for national guidelines for the dosing of MTX in CKD [5, 6].

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Comment on: Kidney disease in RA patients: prevalence and implication on RA-related drugs management: the MATRIX study: reply

SIR, We appreciated the letter from Bateman and colleagues [1]. The case they report emphasizes the risk of MTX use in patients with reduced renal function. In fact, their patient with a Stage 4 renal insufficiency at baseline presented with an episode of functional acute renal failure due to dehydration secondary to diarrhoea. In this particular patient with baseline deeply reduced renal function, the further reduction in glomerular filtration resulted in accumulation, overdosage of MTX and metabolites, resulting in a severe haematotoxicity. In addition, we had previously collected and analysed 10 cases of severe or even fatal MTX toxicity in end-stage renal disease (ESRD) patients after very low MTX doses (<7.5 mg/week) [2], which further emphasize the risk of MTX in RA patients with renal insufficiency.

There is further evidence on the prevalence of renal insufficiency in RA patients. In our MATRIX study, we identified only one patient with Stage 4 kidney disease (Cockcroft and Gault...