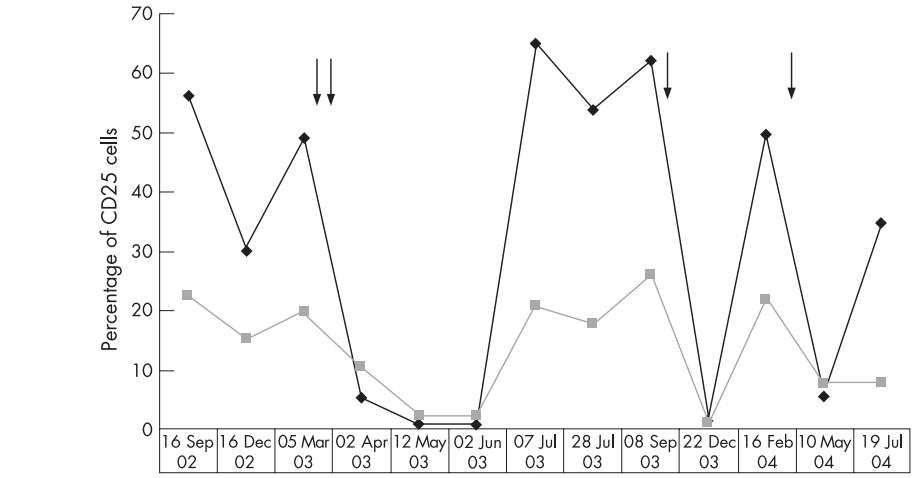

Figure 1 CD4CD25 + and CD8CD25 + cell counts after each infusion.

are depleted.[10] However, we did not detect autoantibodies associated with atrophic gastritis, pernicious anaemia or thyroiditis.

Anti-CD25 treatment induced long-term steroid-free remission in our patient. However, further studies are needed to evaluate the long-term efficacy of anti-CD25 antibody treatment in this and other forms of vasculitis.

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REFERENCES

1 **Van der Ven A**, van Oostenbrugge R, Kubat B, Cohen Tervaert JW. Cerebral vasculitis after initiation antiretroviral therapy. *AIDS* 2002;**16**:2362–4.
2 **Lie JT**. Primary (granulomatous) angiitis of the central nervous system: a clinicopathological analysis of 15 new cases and review of the literature. *Hum Pathol* 1992;**23**:164–171.
3 **Nussenblatt R**, Thompson D, Li Z, Peterson J, Robinson R, Shames R, *et al*. Humanized anti-interleukin-2 (IL-2) receptor alpha therapy: long-term results in uveitis patients and preliminary safety and activity data for establishing parameters for subcutaneous administration. *J Autoimmun* 2003;**21**:283–93.
4 **Przepiorka D**, Kernan N, Ippoliti C, Papadopoulos E, Giralt S, Khouri I, *et al*. Daclizumab, a humanized anti-interleukin-2 receptor alpha chain antibody, for treatment of acute graft-versus-host disease. *Blood* 2000;**95**:83–89.
5 **Renkl A**, Mockenhaupt M, Technau K, Herouy Y, Norgauer J. A novel therapeutic option in pemphigus vulgaris: humanized monoclonal anti-CD 25 antibody. *Br J Dermatol* 2004;**150**:1220–22.
6 **Tomaske M**, Amon O, Bosk A, Handgretinger R, Marion Schneider E, Niethammer D. Anti-CD25 antibody treatment in a child with hemophagocytic lymphohistiocytosis. *Med Pediatr Oncol* 2002;**38**:141–2.
7 **Van Assche G**, Dalle I, Noman M, Aerden I, Swijsen C, Asnong K, *et al*. A Pilot study on the use of the humanized anti-interleukin-2 receptor antibody daclizumab in active ulcerative colitis. *Am J Gastroenterol* 2003;**98**:369–76.
8 **Bielekova B**, Richert N, Howard T, Blevins G, Markovic-Plese S, McCartin J, *et al*. Humanized anti-CD25 (daclizumab) inhibits disease activity in multiple sclerosis patients failing to respond to interferon beta. *Proc Natl Acad Sci USA* 2004;**101**:8705–8.
9 **Hardy G**, Imami N, Sullivan A, Pires A, Burton C, Nelson M, *et al*. Reconstitution of CD4+ T cells responses in HIV-1 infected individuals initiating highly active antiretroviral therapy (HAART) is associated with renewed interleukin-2 production and responsiveness. *Clin Exp Immunol* 2003;**134**:98–106.
10 **Sakaguchi S**, Sakaguchi N, Asano M, Itoh M, Toda M. Immunological tolerance is maintained by activated T cells expressing IL-2 receptor α chains (CD25): breakdown of a single mechanism of self-tolerance causes various autoimmune diseases. *J Immunol* 1995;**155**:1151.

Neutropenia while receiving anti-tumour necrosis factor treatment for rheumatoid arthritis

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Anti-tumour necrosis factor (TNF) α treatment has had a tremendous effect on the managment of rheumatoid arthritis, but it needs to be monitored closely. Guidelines state that haematological complications are rare, so regular full blood counts are not recommended.[1 2] We noticed that a minority of our patients with rheumatoid arthritis receiving anti-TNF treatment developed neutropenia ($<2\times10^9$/l). Table 1 summarises the demographics of 133 patients with rheumatoid arthritis. Of these, 14.3% of patients had at least one episode of neutropenia, with no obvious cause other than the anti-TNF treatment. The lowest neutropenic episodes had counts that ranged from 1.02 to 1.94 (8/19 patients had an episode with

Table 1 Summary of the results of demographics, disease and drug details of patients with and without neutropenia receiving anti-tumour necrosis factor treatment

	Neutropenia ($<2.0\times10^9$/l) (%)	No neutropenia (%)	Statistics
n (%)	19 (14.3)	114 (85.7)	
Female	16 (15.4)	88 (84.6)	$\chi^2=0.47$, p=0.5
Male	3 (10.3)	26 (89.7)	
Mean age (years)	57.4	56.6	t=0.25, p=0.8
Anti-TNF drugs			
Adalimumab	3 (14.3)	18 (85.7)	$\chi^2=0.08$
Etanercept	13(15.3)	62 (84.7)	p=0.96
Infliximab	3 (13.1)	20 (86.9)	
Baseline neutrophil count	3.77	6.12	t=4.85, p<0.001
Baseline total white cell count	5.88	8.82	t=5.23, p<0.001
Neutrophils:white cell count ratio	0.62	0.68	t=2.73, p=0.007
ANA positive	7/65 (10.8)	58/65 (89.2)	$\chi^2=0.001$, p=0.97
ANA negative	4/38 (10.5)	34/38 (89.5)	
On methotrexate	5/47 (10.6)	42/47 (89.4)	$\chi^2=0.79$, p=0.37
Not on methotrexate	14/86 (16.3)	72/86 (83.7)	
On prednisolone	4/53 (7.5)	49/53 (92.5)	$\chi^2=3.2$, p=0.07
Not on prednisolone	15/80 (18.8)	65/80 (81.2)	
Neutropenia on previous DMARDs			
Yes	11/23(47.8)	12/23 (53.2)	$\chi^2=25.5$, p<0.001
No	8/110 (7.3)	102/110 (82.7)	

ANA, antinuclear antibodies; DMARDs, disease-modifying antirheumatic drugs; TNF, tumour necrosis factor.

counts <1.5). The time period between starting anti-TNF treatment and developing neutropenia ranged from 1 week (two patients) to 26 months, with a median of 3 months. Patients with a neutrophil count at baseline <4 had an odds ratio (OR) of 10.7 (95% confidence interval (CI) 3.6 to 31.4) for developing neutropenia. A history of neutropenia when receiving other disease-modifying antirheumatic drugs (DMARDs) gave an OR of 11.7 (95% CI 3.9 to 34.7).

Of the 19 patients, 16 who developed neutropenic episodes while receiving anti-TNF treatment have managed to stay on their original treatment. The usual approach has been temporary cessation, with reinstatement once the neutrophil count has recovered, or in some circumstances a lower tolerated threshold level being set, with no further problems encountered (>1.5). In our experience, patients gain so much benefit from anti-TNF treatment that they are reluctant to stop and are happy to continue, despite the potential risks of neutropenia. However, two of these patients have since had to stop anti-TNF, with one undergoing investigations into the aetiology of a pleural effusion, and another developing a resistant staphylococcal foot infection. One patient who was taking infliximab had recurrent episodes of neutropenia, which were managed with temporary cessation, but subsequently the patient was changed to etanercept and since then has had no further episodes. Another patient changed from etanercept to adalimumab without further problems.

There has been a small number of reports of cytopenias in patients receiving anti-TNF treatment.[1–7] However, no other series of patients have reported a rate of neutropenias affecting 1 in 8 patients, which seems to be the case in our experience. Only one of our patients who developed neutropenia developed a concomitant infection. Our experience of rates of development of neutropenia in patients receiving other commonly prescribed DMARDs such as methotrexate and leflunomide is 12.5% and 14.9%, respectively.[8] In these patients, we perform regular full blood counts, in keeping with national guidelines. The prevalence of neutropenia in patients receiving anti-TNF treatment in our experience is similar at 14.3%, so that it would be inconsistent and unsafe for us not to monitor regular full blood counts in these patients. We would recommend regular full blood counts in all patients receiving anti-TNF treatment, whether they are on concomitant methotrexate or not, and believe that guidelines need to be modified to take this into account. Patients with a baseline neutrophil count <4 and those with a history of neutropenia when receiving DMARDs, need to be monitored particularly closely.

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REFERENCES

1 **Ledingham J**, Deighton C. Update on the British Society of Rheumatology guidelines for prescribing TNFα blockers in adults with rheumatoid arthritis (update of previous guidelines of April 2001). *Rheumatology* 2005;**44**:157–63.
2 **Furst DE**, Breedveld FC, Kalden JR, Burmester GR, Smolen JS, Bijlsma JWJ, *et al*. Updated consensus on biological agents, specifically tumour necrosis factor α, (TNFα) blocking agentsand interleukin-1 receptor antagonist (IL-1ra), for the treatment of rheumatic diseases. *Ann Rheum Dis* 2005;**64**:iv2–14.
3 **Markham A**, Lamb HM. Infliximab: a review of its use in the management of rheumatoid arthritis. *Drugs* 2000;**59**:1341–59.
4 **Jarvis B**, Faulds D. Etanercept: a review of its use in rheumatoid arthritis. *Drugs* 1999;**57**:945–66.
5 **Vidal F**, Fontova R, Richart C. Severe neutropaenia and thrombocytopaenia associated with infliximab. *Ann Intern Med* 2003;**139**:63.
6 **Maini RN**, Breedveld FC, Kalden JR, Smolen JS, Davis D, MacFarlane JD, *et al*. Therapeutic efficacy of multiple intravenous infusions of anti-tumour necrosis factor alpha monoclonal antibody combined with low-dose weekly methotrexate in rheumatoid arthritis. *Arthritis Rheum* 1998;**41**:1552–63.
7 **Kuruvilla J**, Leitch HA, Vickars LM, Galbraith PF, Li CH, Al-Saab S, *et al*. Aplastic anaemia following administration of a tumour necrosis factor-alpha inhibitor. *Eur J Haematol* 2003;**71**:396–8.
8 **Rajakulendran S**, Allen D, Deighton C. Should the monitoring of methotrexate and leflunomide be the same? *Rheumatology* 2005;**44**(Suppl 1):i65.