

Table

Sex	Age (years)	Lumbar (L1-L4)		Femur			
		BMD	Z-score	Neck		Ward's	
				BMD	Z-score	BMD	Z-score
M	16	0.760	-3.01	0.989	+0.11	0.661	-1.42
M	21	0.867	-2.03	1.005	+0.28	0.890	+0.53
F	25	0.885	-1.42	-	-	-	-
M	25	0.915	-1.63	0.945	-0.09	0.766	-0.25

BMD = Bone mineral density (g/cm²)

M = Male

F = Female

The data we obtained suggested that the changes in the bone mineral content in EDS patients, although less intense than in other hereditary collagen diseases, are also present. Our study also suggests that this reduction in bone mass only affects predominantly trabecular bone. Subsequent studies involving greater numbers of patients and a clarification of the biochemical and genetic mechanisms involved in type I EDS should further clarify this subject.

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- 2 Prockop D J. Osteogenesis imperfecta. *Arthritis Rheum* 31: 1-8.
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MATTERS ARISING

G-CSF in gold-induced aplastic anaemia

A letter from MacDonald *et al*¹ reported the case of a 55 year old woman with psoriatic arthritis who developed aplastic anaemia after gold treatment, and was reported to have a less than therapeutic response to filgrastim (G-CSF, Neupogen) therapy. Approximately 30 days after the gold treatment was discontinued, a bone marrow aspirate and biopsy revealed severe aplasia. She was then treated with filgrastim 1.5 mcg/kg on alternate days for three days, then daily for an additional 10 days.

The idiosyncratic myelotoxicity of gold therapy has been well documented and spontaneous neutrophil recovery may take as long as 15 to 30 days after drug withdrawal. Although filgrastim has not been licensed for the treatment of non-cytotoxic drug induced agranulocytosis and the therapeutic dose range for these conditions has not been determined, the standard dose of filgrastim for chemotherapy induced neutropenia has been 5 mcg/kg/day.

Before approval by the Food and Drug Administration, Amgen Inc provided filgrastim to patients with non-cytotoxic drug-induced agranulocytosis in a compassionate use protocol. One of these patients was a 20 year old woman who had developed agranulocytosis after five weeks of gold therapy. For two weeks after the discontinuation of gold treatment the patient had an absolute neutrophil count (ANC) of 0/cmm, and then received filgrastim 10 mcg/kg/day, attaining an ANC of 5100/cmm after four days of filgrastim treatment. Although this was not a controlled clinical trial, this experience demonstrates the activity of filgrastim in enhancing myeloid recovery.² The patient described by MacDonald *et al* may have had an improved response with a higher dose of filgrastim.

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Brother and sister with myeloperoxidase associated autoimmune disease

We read with interest the recent article by Murphy *et al*¹ describing two sisters with

vasculitis associated with antineutrophil cytoplasmic autoantibodies (ANCA). We report a brother and sister with autoimmune disease and circulating antibodies directed against myeloperoxidase.

The brother, aged 77 years, presented with arthralgia, rhinorrhoea and a rapidly deteriorating renal function. A renal biopsy revealed extracapillary focal segmental glomerulonephritis and active vasculitis in a blood vessel. Antinuclear antibodies (ANA), anti-dsDNA, IgM rheumatoid factor and LE-cell test were negative. ANCA were positive with a perinuclear pattern of staining at a titre of 1/64. The antibodies were directed against myeloperoxidase. Treatment with cyclophosphamide and steroids resulted in partial recovery of renal function and the immunosuppressive drugs were tapered. The patient died two years later of myocardial infarction.

The sister presented at the age of 61 with a bilateral pleuritis sicca and arthralgia. ANA were negative, anti-dsDNA (Farr assay) were negative, LE cells were positive (class 5C), IgM rheumatoid factor was negative. ANCA were repeatedly positive with a perinuclear pattern of staining (titre 1/512). ELISA revealed antibodies against myeloperoxidase. She was initially treated with steroids but subsequently needed azathioprine to control recurrent pleuritis sicca and arthralgia. Three years after the first presentation she still requires azathioprine. There has been no evidence of renal disease.

Although the clinical presentation of disease in both siblings differed widely—the brother presented with an idiopathic extracapillary proliferative glomerulonephritis whereas the sister suffered from a lupus like disease—both were found to have circulating antibodies directed against myeloperoxidase. Apart from the recent report in the *Annals*,¹ there has been another communication on ANCA positive vasculitis in siblings: Ten Hacken *et al* reported Wegener's granulomatosis in a mother and daughter, associated with anti-myeloperoxidase antibodies in the former and c-ANCA in the latter.² We agree with Murphy *et al*, that a relatively rare disease like ANCA associated vasculitis within one family suggests a role for genetic factors, although environmental factors may also play a role. Whether family members from patients with ANCA associated disease have an increased prevalence of circulating ANCA, and if this is associated with an increased risk for developing connective tissue disease, remains to be clarified.

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