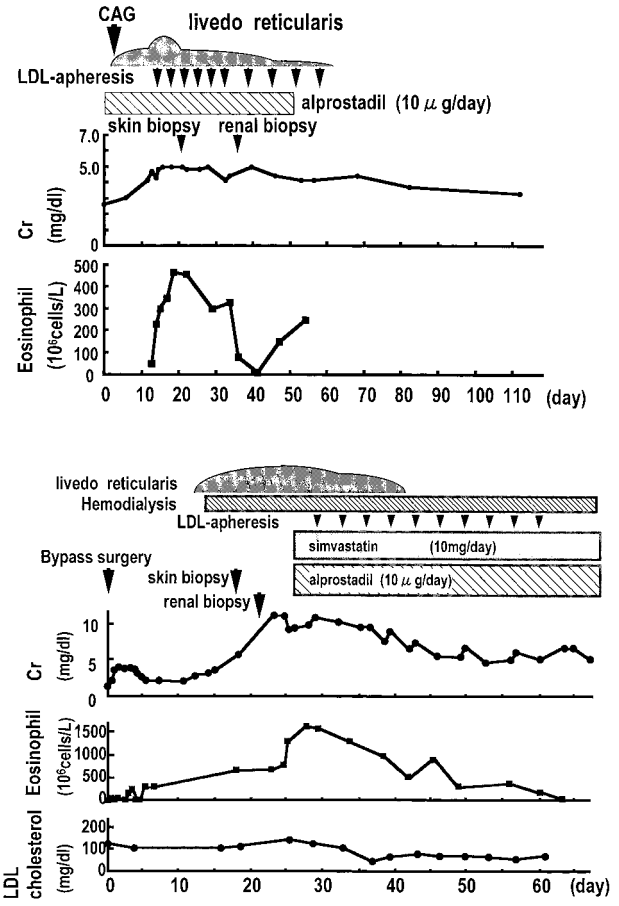

Fig. 1. Clinical course of patient 1 (bottom) and patient 2 (upper).

Patient 2 was a 68-year-old man in whom percutaneous transluminal angioplasty of the femoral artery had been performed 6 months previously and warfarin therapy was begun. He had no coronary risk factors such as diabetes mellitus or cigarette smoking. He was admitted with bilateral painful acrocyanosis and a serum creatinine concentration of 2.6 mg/dl with almost normal sized kidneys. On the second day after admission, coronarography and femoral angiography were performed by the brachial artery approach. After angiography, acrocyanosis worsened and 10 days later, marked livedo reticularis of the trunk and lower extremities appeared along with an increase in the serum creatinine concentration. The progressive renal dysfunction and livedo reticularis were thought to result from CE, and LDL apheresis was performed at once. Following apheresis, the level of consciousness improved and livedo reticularis improved in parallel as did the pain from the acrocyanotic toes. Renal function did not recover, however, cholesterol crystals were noted in skin and kidney biopsy specimens.

In CE patients as well as arteriosclerosis obliterans, the short-term effect of LDL apheresis on ischaemic toe pain, livedo reticularis and level of consciousness can be interpreted mechanistically as follows; (i) improvement of blood and plasma viscosity, and of deformability of red cells secondary to reduction of lipoprotein concentrations, (ii) generation of bradykinin, nitric oxide derivatives [4] and prostaglandins (PG) e.g. PGE_2 and PGI_2, secondary to improved hemorheology and microcirculation [5]. Recently single sessions of LDL apheresis have been reported to improve endothelial function by reducing the concentration of total LDL and oxidized LDL [6]. LDL apheresis may be more beneficial for CE induced damage in skin and brain than kidney. In the former tissues collateral arteries can develop. After recovery, it does make sense to treat with simvastatin or alprostadil concommitantly with LDL apheresis. Renal failure due to CE is progressive and carries an extremely poor prognosis. Even in surviving patients, it generally takes over 8 months to recover renal function and discontinue HD [7]. Renal function may recover after restoration of a blood supply to damaged but viable glomeruli.

Acknowledgements. We wish to thank the following doctors for help in the treatment of these patients and for providing biopsy samples. H. Araki, MD, T. Matsuda, MD, T. Kinbara, MD, Y. Fujita, MD, R. Tatami, MD, H. Hanakawa, MD, N. Otsuki, MD, M. Namura, MD and I. Koni, MD.

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1. Donald GV. Cholesterol emboli: A common cause of renal failure. *Annu Rev Med* 1997; 48: 375–385
2. Cabili S, Hochman I, Goor Y. Reversal of gangrenous lesions in the blue toe syndrome with lovastatin—A case report. *Angiology* 1993; 44: 821–825
3. Mabuchi H, Michishita I, Takeda M *et al.* A new low density lipoprotein apheresis system using two dextran sulfate cellulose columns in an automated column regenerating unit (LDL continuous apheresis). *Atherosclerosis* 1987; 68: 19–25
4. Kojima S, Harada-Shiba M, Yamamoto A. Plasma constituents other than low-density lipoprotein adsorbed by dextran-sulfate column. *Therapeutic Apheresis* 1997; 1: 309–313
5. Kojima S, Ogi M, Sugi T *et al.* Changes in plasma levels of nitric oxide derivative during low-density lipoprotein apheresis. *Therapeutic Apheresis* 1997; 1: 356–361
6. Tamai O, Matsuoka H, Itabe H *et al.* Single LDL apheresis improves endothelium-dependent vasodilatation in hypercholesterolemic humans. *Circulation* 1997; 95: 76–82
7. Mannesse CK, Blankestijn PJ *et al.* Renal failure and cholesterol crystal embolization: a report of 4 surviving cases and a review of the literature. *Clin Nephrol* 1991; 36: 240–245

Does colchicine also induce a clearance of the established amyloid deposits?

Sir,

The issue of whether amyloid deposits are cleared is still controversial. We had the opportunity to follow a case which is relevant in this context.

Case. A 26-year-old woman was admitted to our hospital in 1989 for the evaluation of a massive anasarca-type pitting oedema that had become apparent over the month before admission. She also had a 6-month history of frothy urine. She was married for 11 years but had no pregnancy in that time. On physical examination she had signs of pleural effusion, ascites, hepatomegaly as well as massive peripheral and sacral pitting oedema. The positive laboratory findings included a microcytic anaemia with a haemoglobin of 8.5 g/dl and MCV of 72.2; ESR was 120 mm/h and total serum protein and albumin levels were remarkably low with values of 4 g/dl and 2 g/dl, respectively. Urinary protein excretion (24-h) was 7 g/day and creatinine clearance was 75 ml/min. ANA, HBsAg, antiHCV were all negative. Abdominal ultra-

sound revealed slight enlargement of both kidneys (right kidney: 111×50 mm; left kidney: 138×50 mm) with increased echogenicity in parenchyma and a 5×4 cm mass lesion in the portal area. A renal biopsy, an excisional biopsy of the mass as well as a biopsy from the nearby enlarged lymph nodes were performed and all of them revealed amyloidosis. The diagnosis of AA amyloidosis was confirmed by potassium permanganate stain. Bone marrow biopsy that was performed showed only bone marrow hyperplasia. Her oedema improved after she was started on diuretics and after the institution of colchicine in the dose of 1.5 mg/d she was discharged to follow-up. A decrease in proteinuria was observed with 24-h urinary protein excretion decreasing to 2 g/day by July 1990. After she was started on colchicine therapy, she had two successful pregnancies in 1991 and 1993 which she delivered uneventfully on term. Repeated ultrasound examination of the abdomen in 1994 showed the decrease in the size of both kidneys (right kidney: 108×40 mm; left kidney: 117×50 mm). Her renal function improved with a creatinine clearance of 95 ml/min, and proteinuria was 0.5 g/day. She remained on follow-up and by March 1998 her 24-h urinary protein excretion had come down to nil. The repeated renal biopsy that was performed revealed scarcely distributed amyloid in the glomeruli with the significant decrease in the amount of amyloid deposits compared to previous biopsy.

Comment. Amyloidosis secondary to familial Mediterranean fever (FMF) may occur in patients who present with only mild or occasional attacks or even in those who never experienced an acute febrile episode before [1–4]. Although our case did not have previous history of characteristic FMF manifestations, the fact that she originated from central Anatolia region led us to suspect FMF. There is an unexplained difference in the prevalence of amyloidosis among the different ethnic groups of patients with FMF [2,5]. In Turks, amyloidosis reaches an incidence of 60% among the subjects affected by FMF [5]. In the patients with a well-established amyloidosis, colchicine may induce complete remission of proteinuria or the nephrotic syndrome that can last as long as 10 years [4,6]. It is well known that colchicine prevents the development of amyloidosis in almost all patients compliant to therapy and also reverses the clinical manifestations of organ involvement in established amyloid cases [1,2]. However, it is generally believed that although the amyloidosis seems to be clinically cured by colchicine therapy, a large amount of amyloid deposits still remains in the involved organs [5]. Our case demonstrated that colchicine therapy in this patient with the frank, biopsy-proven amyloidosis of both the kidneys and the liver not only improved her clinically and enable her to become fertile but also induced a decrease in the amount of deposited amyloid that was demonstrated on the repeated renal biopsy. We concluded that colchicine does not only prevent the FMF attacks, the subsequent development of secondary amyloidosis and the reversal of the clinical picture but also seems to induce the clearance of amyloid deposits in the previously involved organs.

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1. Friman C, Pettersson T. Amyloidosis. *Current Opin Rheumatol* 1996; 8: 62–71
2. Ben-Chetrit E, Levy M. Familial Mediterranean fever. *Lancet* 1998; 351: 659–664
3. Goldfinger SE. Colchicine for familial Mediterranean fever. *N Engl J Med* 1972; 287: 1302–1306
4. Livneh A, Langevitz P, Zemer D *et al.* The changing face of familial Mediterranean fever. *Semin Arthritis Rheum* 1996; 26: 612–627
5. Pras M, Bronshpigel N, Zemer D *et al.* Variable incidence of amyloidosis in familial Mediterranean fever among different ethnic groups. *John Hopkins Med J* 1982; 150: 22–26
6. Skinner M, Anderson JJ, Simms R *et al.* Treatment of 100 patients with primary amyloidosis: A randomized trial of melphalan, prednisone and colchicine versus colchicine only. *Am J Med* 1996; 100: 290–298

Defective erythropoietin production in the anaemia of malaria

Sir,

Falciparum malaria is one of the most common parasitic diseases causing high morbidity and mortality in the tropics. The origin of malaria-induced anaemia is quite complex including: red blood cell destruction and phagocytosis, hyperplenism, autoimmune mechanisms, inhibition of red cell production, ineffective erythropoiesis due to release [1] of interferon gamma and tumour necrosis factor, and interleukin 1 despite an increase in erythropoietin (Epo) production [2]. The aim of the present study was to evaluate serum Epo levels in patients suffering from acute *Plasmodium falciparum* infection to gain insight into Epo response to different degrees of anaemia.

The study was performed at the Sololo Catholic Hospital (Kenya, East Africa) and the Bissau Simon Mendez Hospital (Guinea Bissau, West Africa).

Fifty-two patients (26 males and 26 females; age range 1–37 years) took part in the study. Microscopy on thick blood film lead to a diagnosis of *P falciparum* malaria in all cases. Patients were treated both as either as (i) ambulatory outpatients (uncomplicated malaria) with oral amodiaquine or sulfadoxine + pyrimethamine or (ii) severe inpatients (complicated malaria) with intravenous quinine.

Blood samples were taken at the time of admission to determine serum haemoglobin and Epo. Epo levels were evaluated by *in vitro* enzyme-immunoassay (Quantikine IVD, R & D System, Minneapolis, MN, USA); normal Epo values were 3.3–16.6 mIU/ml. Statistical analysis was performed by regression line and Pearson's correlation coefficient.

The results showed severe anaemia (Hb < 5 gr/dl) in 4 of 52 patients (7.7%), moderate anaemia (Hb 5–8 gr/dl) in 19 (36.5%), mild anaemia (> 8 gr/dl) in 18 (34.6%) and normal Hb values in 11 patients (21.2%), according to the anaemia classification of Clinical Guidelines [3]. 43.5% of the cases with severe or moderate anaemia occurred in malaria patients under the age of 9 and another 34.8% of these cases occurred during pregnancy. Anaemia secondary to malaria was an important cause of hospital admissions in children and pregnant women.

Patients received antimalaria drugs and both iron and folic acid. None of the patients had acute or chronic renal failure. Nevertheless, in some cases severe or moderate anaemia did not improve but rather persisted despite pharmacological treatment. The Epo and Hb values for each patient are indicated by the squares in Figure 1.

The mean of Epo value was 264.6 ± 530.24 mU/ml (range 5.4–3094). Moreover, in all of the cases considered, there was a good inverse correlation between log-Epo and Hb: $\log[\text{Epo}] = 3.133 - (0.148 \times \text{Hb})$; $r = 0.607$; $P < 0.001$. This demonstrated that in falciparum malaria anaemia is an efficient stimulus for Epo generation.