endogenous interferon-γ and chronic activation of the cellular immune system.

Several observations on soluble markers for cellular immune activation support this idea. Concentrations of sTNF-R are positively correlated with those of neopterin, an indicator of T cell/macrophage activation in patients with haematological neoplasia[3] and other illnesses. Neopterin concentrations in patients with various malignancies consistently provide significant, independent prognostic information.[4] Moreover, immune activation itself may contribute to free-radical-mediated processes leading either to enhanced cell proliferation by activation of nuclear factors, or to programmed cell death (eg, via neopterin[5]).

Immune activation in cancer may not be solely beneficial; when chronic immune activation is present while normal immune effector functions are lacking the long-term actions of cytokines upon cells may have adverse consequences. Our hypothesis together with the explanation suggested by Langkopf and Atzpodien, may represent a scenario in which the immune system could even support tumour progression.

Gilbert Reibnegger, Antonio Diez-Ruiz, Dietmar Fuchs, Helmut Wachter

Institute of Medical Chemistry and Biochemistry and Ludwig-Boltzmann Institute of AIDS Research, University of Innsbruck, A-6020, Austria

1 Lantz M, Malik S, Slevin ML, Olsson I. Infusion of tumor necrosis factor TNF causes an increase in circulating TNF-binding proteins in humans. *Cytokine* 1990; **2:** 402–06.

2 Aderka D, Engelmann H, Maor Y, Brakebusch C, Wallach D. Stabilization of the bioactivity of tumour necrosis factor by its soluble receptor. *J Exp Med* 1992; **175:** 323–29.

3 Denz H, Orth B, Weiss G, et al. Serum soluble tumour necrosis factor receptor 55 is increased in patients with haematological neoplasia and is associated with immune activation and weight loss. *Eur J Cancer* 1993; **29A:** 2232–35.

4 Reibnegger G, Fuchs D, Fuith LC, et al. Neopterin as a marker for activated cell-mediated immunity: application in malignant disease. *Cancer Det Prev* 1991; **15:** 483–89.

5 Weiss G, Fuchs D, Hausen A, et al. Neopterin modulates toxicity mediated by reactive oxygen and chlorine species. *FEB Lett* 1993; **321:** 89–92.

Anaphylactic reactions to liposomal amphotericin

SIR—Liposomal preparations of amphotericin B have the advantage of much lower toxicity compared with conventional preparations.[1] For this reason, clinicians may prefer liposomal preparations, such as AmBisome, for treatment of fungal infections in severely ill patients. We report anaphylaxis to AmBisome in 2 patients who were not allergic to amphotericin.

A 29-year-old man, who had developed AIDS 31 months earlier, was admitted to hospital with dysphagia secondary to endoscopically proven oesophageal candidosis. His admission medication was co-trimoxazole, prednisolone, glipizide, acyclovir, omeprazole, thalidomide, and paroxetine. His dysphagia did not respond to successive courses of intravenous fluconazole and oral itraconazole and he had also received topical clotrimazole and amphotericin lozenges with no benefit. Sensitivity testing of the candidal isolate revealed diminished sensitivity to the triazoles and it was therefore decided to alter treatment to amphotericin in the form of AmBisome (dose 1 mg/kg). 5 mL of AmBisome (Vestar) had been infused when the patient developed an anaphylactic reaction of hypotension, erythema, fever, bronchospasm, and facial oedema. The AmBisome was discontinued and he recovered after administration of intravenous adrenaline (1 mL of 1 in 1000) and hydrocortisone 200 mg. 1 week later, conventional amphotericin B was infused at a dose of 0·3 mg/kg without adverse reaction.

A 25-year-old woman was admitted to hospital after a subarachnoid haemorrhage complicated by acute hydrocephalus. A ventricular access device was inserted on admission and 1 month later she became febrile and was found to have *Candida albicans* meningitis. The ventricular access device was replaced and treatment started with flucytosine 250 mg/kg (dose adjusted in response to serum drug concentrations) and amphotericin 0·7 mg/kg which she tolerated well. 24 days subsequently, after little clinical improvement, the antifungal regimen was changed to flucytosine 250 mg/kg and AmBisome 3 mg/kg. At that time she was also on phenytoin, chlorpromazine, and ranitidine. Within 30 s of starting AmBisome, she developed severe bronchospasm, cyanosis, and widespread erythema which resolved after stopping the infusion and administration of intravenous hydrocortisone 100 mg. Subsequent treatment with amphotericin was again tolerated without adverse reaction.

AmBisome is a unilamellar liposomal preparation of amphotericin[2] which has proved effective in the treatment of fungal infections including candida, aspergillus, and cryptococcus.[3] Fusion of the liposome vehicle with the fungal cell membrane is thought to result in a more efficient uptake of amphotericin by the fungus.[4] Adverse reactions to amphotericin have included hyperpyrexia, hypotension, renal tubular damage, hypokalaemia, anaemia, and hepatitis.[5] By contrast, AmBisome has been associated with a low number of adverse reactions and there is little evidence of renal toxicity, which has resulted in the drug being favoured for use in the severely ill patient with fungal infections. We report anaphylactic reactions to AmBisome in 2 patients being treated for systemic candidosis. The AmBisome infusions were prepared, by two different hospital pharmacies, according to the manufacturer's guidelines. It is noteworthy that both patients received intravenous amphotericin with no allergic reaction after treatment with AmBisome was withdrawn. It is therefore probable that the lipid component of the drug caused the immediate, potentially fatal, reactions. We suggest that initial treatment with AmBisome should only be given under close medical supervision in hospital where facilities for resuscitation are immediately available. Furthermore, a test dose of the drug, as recommended for amphotericin, could be of use in discerning those at risk of an anaphylactic reaction to AmBisome. In our experience, anaphylaxis or severe allergic reactions to AmBisome do not preclude the subsequent use of amphotericin.

R B S Laing, L J R Milne, C L S Leen, G P Malcolm, A J W Steers

Regional Infectious Disease Unit, City Hospital, Edinburgh EH10 5SB, UK; Department of Mycology, Western General Hospital, Edinburgh; and Department of Clinical Neurosciences, Western General Hospital

1 Meunier F, Prentice HG, Ringden O. Liposomal amphotericin B (AmBisome): safety data from a phase II/III clinical trial. *J Antimicrob Chemother* 1991; **29** (suppl B): 83–91.

2 Adler-Moore JP, Proffitt RT. Development, characterisation, efficacy and mode of action of AmBisome, a unilamellar liposomal formulation of amphotericin B. *J Liposome Res* (in press).

3 Ringden O, Meunier F, Tollemar J, et al. Efficacy of amphotericin B encapsulated in liposomes in the treatment of invasive fungal infections in immunocompromised patients. *J Antimicrob Chemother* 1991; **28** (suppl B): 73–82.

4 Adler-Moore JP, Fujii G, Lee MJA, et al. In vitro and in vivo interactions of AmBisome with pathogenic fungi. *J Liposome Res* **3:** 151–56.

5 Miller R, Bates JH. Amphotericin B toxicity: a follow up report of 53 patients. *Ann Intern Med* 1969; **71:** 20–27.