Ellis and Cunningham cite a study in which patients were randomised to fluorouracil-doxorubicin-methotrexate or to best supportive care.² They comment that randomisation was stopped in mid-study because of the apparent survival benefit in the chemotherapy arm. Subsequent patients recruited to the study were assigned only to the chemotherapy arm. Only 10 patients had been accrued in the control group and 12 in the treatment arm when randomisation was stopped. No formal assessment of quality of life was included.

Randomisation of the number of patients agreed before a study is started is aimed at ensuring that the comparability of the treatment groups is valid and that any confounding variables (in this case general medical condition and bulk of disease) are adjusted for. If randomisation is stopped prematurely, as in this study, the bias of the non-random sample is not discounted. Better quantitative and qualitative data are required to support the value of palliative chemotherapy in advanced gastric cancer over supportive care alone. I hope that future studies will systematically include measurement of quality of life.

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Asylum seekers in Britain

EDITOR,—In her news article Claudia Court states that 700 people are seeking asylum in Britain¹; this is a considerable underestimate. The Home Office's latest figures show that 45 800 people were waiting for their applications to be processed at the end of 1993 (personal communication). To achieve the coveted status of refugee applicants have to demonstrate a well founded fear of persecution, usually because of religious or political beliefs; only 3% succeeded in 1992. The number of asylum seekers in detention varies but can rise to 950 despite there being only 450 places. Many of the rest are confined in prison—a practice that the chief inspector of prisons, Judge Tumim, recently expressed grave doubts about. His description of the detainees he saw in Pentonville prison—"distressed, despondent, and in some cases desperate"—is vivid. Four asylum seekers have committed suicide since 1987, and others have made serious attempts at suicide.

The countries of origin of most detainees seeking asylum have been reported by Amnesty International as being subject to civil war, political turmoil, or torture and murder of members of opposition parties. The Medical Foundation for the Care of Victims of Torture finds that most alleged victims of torture are genuine. Many, rather than exaggerating, play down their experiences. Falanga (beating the soles of the feet) is so common that many do not think to mention it, and both men and women may be so ashamed of having been sexually abused that they have to be persuaded to admit it. The destructive effect of the torture on the victim's family relationships often provides supportive evidence of what has taken place.

The increase in refugees requesting the foundation's help since the passage of the Asylum Act 1993 has obliged it to develop a training course to enable doctors to establish new support centres outside London. Currently referrals come from all over Britain, so some patients are compelled to travel huge distances, especially when follow up interviews are necessary. The course organiser,

Dr Gill Hinshelwood, is adamant that interested doctors should not feel intimidated at the idea of examining victims of torture. They should start with what they can manage and develop a service that responds to local needs in whatever way they can. The staff of the foundation are always available to advise over the telephone if there are any problems.

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1 Court C. Asylum seekers run high risk of detention in Britain. *BMJ* 1994;308:811. (26 March.)

Snoring and sleep apnoea

EDITOR,—In his letter on the management of snoring Peter J Robb states that treatment by uvulopalatopharyngoplasty is associated with minimal morbidity and mortality in selected patients.¹ This may not be the case.

Some "simple snorers" can develop sleep apnoea just by gaining weight, and others seem to develop sleep apnoea with advancing years for unrecognised reasons. In people with sleep apnoea obstruction occurs at either the retroglossal or the retropalatal level,^{2,4} and treatment with continuous positive airway pressure requires a seal between the soft palate, palatal arches, and tongue. Thus, after uvulopalatopharyngoplasty a patient who develops sleep apnoea with retroglossal obstruction may be untreatable by continuous positive airway pressure owing to loss of the palatal seal. The patient will therefore be at risk of the cardiovascular morbidity and death associated with sleep apnoea,⁵ as well as the increased risks associated with driving unless tracheostomy is performed.

Until more is known about the aetiology and natural course of sleep apnoea, operative treatment of snoring by uvulopalatopharyngoplasty even in selected patients may be associated subsequently with appreciable morbidity and death.

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4 Stein MG, Gamsu G, De Greer G, Golden JA, Crumley RL, Webb WR. Cine CT in obstructive sleep apnoea. *Am J Radiol* 1987;148:1068-74.

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Human gonadotrophin preparations

May cause allergic reaction

EDITOR,—We were interested in the letter from Aliza Eshkol, of Ares-Serono Group, and Mercia L Page, of Serono Laboratories (UK), regarding extraneous active substances in the old gonadotrophin preparations derived from urine.¹ We have noticed that some patients undergoing ovarian stimulation with human menopausal gonadotrophin (Pergonal (Serono)) in our in vitro fertilisation programme develop symptoms that suggest an allergic reaction. The symptoms may be systemic or localised to the injection site, as described by other centres.² Despite this reaction the patients' ovaries seem to respond normally to stimulation with gonadotrophin, which led us to hypothesise that the non-gonadotrophin proteins

(more than 95% of the total protein content³) could be responsible for stimulating an immune response.

Two of these patients presented for a subsequent cycle of treatment, for which we used a new highly purified follicle stimulating hormone preparation (Metrodin high purity, Serono). Both patients responded well without any symptoms. During cycles in which human menopausal gonadotrophin had been given in combination with a subcutaneous depot of goserelin (case 1) and intranasal buserelin (case 2) they had developed weals at the site of injection of the gonadotrophin, pyrexia, oedema of the face and hands, photophobia (case 1), and fever with flu-like symptoms (case 2). Before treatment with the highly purified follicle stimulating hormone preparation we collected 10 ml plasma for investigation, and an assay was devised to find out whether IgG antibodies to the human menopausal gonadotrophin preparation were present.

Microtitre plates were coated with the human menopausal gonadotrophin, and serum from the patients was serially diluted (1:10 to 1:2430) across the plates. After two hours' incubation, the plates were washed and a Fab specific, IgG antibody labelled with peroxidase was added at a dilution of 1/300. Substrate was added, and the plates were read with a dual wavelength reader. The two patients had considerably increased levels of IgG antibodies to human menopausal gonadotrophin compared with 10 normal control patients. Higher levels were seen in the patient in case 2, who had not been exposed to the gonadotrophin for 18 months, the patient in case 1 had been exposed to the gonadotrophin five months previously.

Further studies on patients treated with this human menopausal gonadotrophin without reaction are being pursued. These initial results suggest, however, that components of the preparation—perhaps the biologically active proteins referred to by Eshkol and Page—are antigenic in at least some patients and may provoke an immune response. The adverse effects of this response put further stress on the patient at an already difficult time, and the introduction of a purified gonadotrophin preparation is a welcome development for these patients.

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2 Li TC, Hindle JE. Adverse local reaction to intramuscular injections of urinary derived gonadotrophins. *Hum Reprod* 1993;8:1835-6.

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Use luteinising hormone also

EDITOR,—We wish to comment on the two letters about human gonadotrophin preparations.^{1,2} Although Metrodin (urofollitrophin) high purity (Serono, Welwyn Garden City) is considered a state of the art drug by the manufacturers,³ we have reservations about the use of preparations containing follicle stimulating hormone alone in ovarian stimulation. Luteinising hormone may have a more important role in follicular development than previously considered in superovulated cycles. In this unit we noted a considerable drop in success on changing from human menopausal gonadotrophin (Pergonal; Serono) to urinary follicle stimulating hormone (Metrodin; Serono) and Metrodin high purity. We perform about 160 cycles of in vivo fertilisation a year. In 1993