patients have coinfection with HIV. Poor health-care management and a disrupted society seem to account for the worsening epidemiological situation. The professional skill of physicians and nurses is, I believe, equal to that of the west, but the health-care administration is disastrous and communication networks are badly structured and inefficient. For these reasons I would like to invite those with an interest in TB to come and work with us. We can share with them our willingness to act.

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SIR—Few organisations from the West have first-hand experience of the difficulties of controlling tuberculosis (TB) in the former Soviet Union. Burns and colleagues mention the problems faced by a team from Project Hope who are working on TB in Atyrau, Kazakhstan. MERLIN (Medical Emergency Relief International) has similar experience in the Tomsk region in Siberia.

Cure rates in Tomsk tend to be low. The incidence of new cases of TB in 1993, in a population of about 1000 000, was 53 per 100 000 and the prevalence was 390 per 100 000 (although this figure might contain some cases with inactive disease). The wide discrepancy between incidence and prevalence suggests that there is a large pool of chronic cases who could pose a major clinical social and economic problem. Among different groups, the incidences were highest in the most socially disadvantaged (reaching 400 per 100 000 in prisoners) and among men between the ages of 20 and 49.

The team working in Atyrau reported high levels of resistance to antituberculosis drugs and similar results were found in Tomsk. However, the methods used to measure resistances in the Tomsk area are not standard, and a collaborative study between MERLIN and the laboratories in Tomsk has been set up. Isolates from patients in Tomsk have been brought to the UK for analysis by a reference laboratory.

Multidrug resistance and low cure rate can probably be attributed to the treatment regimens in the Tomsk area. The regimen calls for three drugs to be given for two or three months, depending on the patient's condition. The drugs may be changed during this period. Patients are then declared inactive and are given two months' isoniazid monotherapy in spring and autumn for the following two years. Drug shortages mean that the initial treatment is often intermittent and incomplete. As an adjunct to drug therapy, and in relapse, other treatments include intrabronchial instillation of isoniazid (via a Foley catheter passed down the nose) and galvanisation (application of a weak electric current across the chest during intravenous isoniazid). If there is no cure after these treatments (defined locally as closure of cavities on radiography) then 28% of patients undergo thoracic surgery, mostly lobectomy.

The TB physicians in the Tomsk region are able and committed, but are frustrated by inadequate drug supplies. Screening and preventive services consume large amounts of resources. Children receive BCG five days after birth and thereafter receive an annual Mantoux test. Individuals may be given BCG every seven years until they are 35. All adults are supposed to be screened annually by mass miniature radiography but the uptake is much higher by the urban employed than by risk groups—the unemployed, the homeless, and the elderly. The microbiology services are primitive, under-resourced and under-used. The MERLIN programme, which has been approved by WHO, is offering information and resources to physicians in Tomsk to adopt WHO protocols and strategies for diagnosis and treatment. With funding from the European Commission and Glaxo, we have supplied sufficient drugs for all patients in the region for 3 years and are re-equipping the microbiology services. We agree with Burns and his colleagues that financial support for national TB programmes in Russia and the former Soviet Union is vital. We believe that the West should take a leading role in providing both funding and information.

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Effect of Edmonston-Zagreb high-titre vaccine on nutritional status

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SIR—Our original study in Senegal showed that high-titre measles vaccines were increasing the risk of death of children,[1] although the vaccines provided a significant protection against the disease.[2] After our publication, WHO asked for an independent comparative analysis of available data, which confirmed our findings. Since then, WHO no longer recommends the use of the Edmonston-Zagreb high-titre vaccine (EZ-HT).[3]

The negative effect of the EZ-HT vaccine on child survival seemed to be higher for girls than for boys. The sex differences were not significant in our study (relative risk [RR]=1·20, p=0·497 in the EZ-HT group), but were found to be similar in other studies. When examined by sex, the differences in mortality in the Senegal study were significant for female children but not for male. In a sense, this finding was expected since measles shows an excess female mortality worldwide.[4] However, we felt that the vaccines were also deleterious for male children.

Data showing an effect of the EZ-HT vaccine on nutritional status are now available.[5] The study was conducted among the survivors of the participants in the original study, and in fact was a natural follow-up of the randomised vaccine trial and took place within two months after the updating of the survival status in October, 1990. Children born between Feb 1, 1988, and Sept 30, 1988 (monthly birth cohorts 13–20), who had received the EZ-HT at 5 months or the standard Schwarz vaccine at 10 months, who were still resident, were investigated in November and December, 1990. Their weight, height, and arm circumference were measured by trained personnel. Age was known for all children. Standardised indices of nutritional status (Z-score) were computed with the US national (NCHS) standard: height for age, weight for age, weight for height. A cutoff of –2 SD was taken as the threshold for poor nutritional status. Since the children were aged 26–33 months (when arm circumference is virtually constant) the plain value of arm circumference was used, and the standard cutoff of 125 mm was taken as a criterion for poor nutritional status.

There was no excess prevalence of stunting (height for age lower than –2 SD) in the group that received EZ-HT vaccine (RR 1·03, 95% CI 0·88–1·21, p=0·711). However, there was a major effect on wasting. Children who had received EZ-HT vaccine at 5 months had 2·85 times more chance of being under the –2 SD thresholds of weight for height than their counterparts who received the standard vaccine at 10 months (95% CI 1·34–6·06, p=0·007). Similarly, children who received the EZ-HT vaccine at 5 months were 1·36 times more likely to be under the –2 SD threshold of weight for age than control children (1·10–1·68, p=0·005). Differences according to arm circumference were in the same direction, but were not statistically significant. However, all 5 children with an arm circumference lower than 110 mm (severe malnutrition) were in the EZ-HT group (p=0·001).*

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More importantly, both sexes showed a consistent and similar increase in wasting (low weight for height) in the EZ-HT group. Here, the differences were more striking in males and significant only among males. (3·16, 1·17–8·57, p=0·023). The same was true for weight for age (1·41, 1·05–1·89, p=0·023). The differences may look small: for instance, 49 per 1000 in the EZ-HT group versus 17 per 1000 for low weight for height. However, assuming that this difference reveals a group of children at high risk of death, this will be translated into an absolute difference of 32 per 1000, which is similar to the absolute difference in mortality between the two groups (47 per 1000 at age 30 months). The fact that a low nutritional status seemed to be more pronounced in boys may be attributable to a selection effect. Since girls were more likely to die before the nutritional assessment, the sample may have been biased towards fewer surviving girls and more surviving boys suffering from the late effect of the vaccine. In any case, these findings underline the fact that the EZ-HT vaccine was deleterious at the same time for both sexes and that stopping its use for everybody was wise.

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*Table of full results available from *The Lancet* or from the author, on request.

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Frequency of infection in plateau-phase multiple myeloma

SIR—Chapel et al (April 30, p 1059) report a small randomised trial evaluating the effect of prophylactic intravenous immunoglobulin in the prevention of infection in plateau-phase multiple myeloma. As rationale for this trial they cite an earlier study in which they found that three-quarters of all serious infections in myeloma patients occurred more than three months after diagnosis and initial chemotherapy.[1] Other workers'[2] and our own data do not, however, support this observation.

We evaluated the frequency of infection in 114 patients followed for 2892 plateau months (mean 25·1, range 1·5–157). With Chapel and co-workers' criteria, there were four episodes of septicaemia, three of pneumonia, and four of other serious infections in 8 patients (7%), with a frequency of one serious or life threatening infection every 271 plateau months. Our practice is not to routinely use prophylactic intravenous immunoglobulin and to reserve this agent for patients with confirmed recurrent bacterial infections.[3] In fact, in this cohort of plateau-phase patients, only 1, with recurrent respiratory tract infection, fulfilled these criteria and was receiving both prophylactic immunoglobulin and antibiotics. By contrast with our data, the frequency of such infections in the placebo arm of Chapel's study was one infection every 12·4 months, whereas in the immunoglobulin arm it was one infection per 26·2 months.

One explanation for this striking discrepancy in infection rates might be patient selection and the definition of plateau. Despite the title of their article, only 44 of Chapel and colleagues' patients actually fulfilled one of the key criteria for plateau phase—ie, stable paraprotein for at least 6 months. The others were thought to have stable disease, although the exact definition of this state is not provided. By contrast, all our patients were assigned to plateau-phase by standard criteria.[4]

Our data, unlike those of Chapel, indicate that in true plateau-phase myeloma the incidence of serious bacterial infection is very low and would not justify the routine use of prophylactic intravenous immunoglobulin. Patients with recurrent documented bacterial infection (especially polysaccharide encapsulated bacteria) may, however, benefit from such therapy.

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Arthropathy in thalassaemia patients receiving deferiprone

SIR—Berkovitch and colleagues (June 11, p 1471) report three further cases of arthropathy in patients receiving the oral iron chelator L_1 (deferiprone). This complication was first reported in 4 of 13 cases treated by Bartlett and co-workers,[1] and subsequent cases have been described (refs 2, 3, and Al-Refaie et al. *Br J Haematol* 1994; **86** (suppl 1): 5 (14)). Berkovitch and colleagues conclude by stating that future trials of deferiprone will show the frequency of arthropathy in larger numbers of patients. There are now at least eight published reports of long-term trials of deferiprone therapy recently reviewed and updated[4] giving an overall frequency of arthropathy of 16·5% (41 of 248 patients).

Berkovitch and co-workers' findings also accord with those of previous reports[2,3] that there is no correlation between the presence or not of arthropathy and positive tests for antinuclear factor or rheumatoid factor. They state that synovial fluid aspirated from the joints in their patients revealed "low concentrations of deferiprone uncomplexed to iron". They provide no data for synovial fluid deferiprone concentrations, nor do they mention how deferiprone was detected and measured, or how free, glucuronidated, and iron-complexed deferiprone were distinguished. It is unclear when deferiprone was taken by mouth in relation to the time of joint aspiration. There is no mention of the relation of synovial fluid deferiprone concentration to the simultaneous serum concentration of deferiprone. In a previous abstract[5] they stated that synovial deferiprone concentrations were similar to those in serum, iron complexes being undetectable. Whether the arthropathy is caused by the formation of 1/1 and 1/2 iron/deferiprone complexes capable of generating free radicals (as Berkovitch suggests) or to