Nations scholarships. In many cases, students are supported by families who are not rich and who are making every kind of sacrifice to get their sons or daughters through medical school. We have students who try to make it on their own money and have to take a year off to earn money to return to school. I hope these are enough examples to eliminate the idea that we are just catering to rich students.

There is no doubt that approval by the British medical establishment, and especially the GMC, would enormously help St George's to realise its goal of becoming an international school. It would not only greatly increase our intake from the developing world, especially from Africa and Asia, but it would open up our acceptance by the most advanced hospitals in the Caribbean and promote another of our dreams—that of concentrating most of our primary clinical training in the Caribbean.

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SIR,—I am glad that the story of St George's University Medical School has been told (24 July, p 276), but surely the most essential victims of this exercise are the NHS patients who are being used as teaching fodder? Grenadian students come to Britain to practise on NHS patients because there are not enough patients to go round in Grenada. I know of no NHS patient who has been asked to approve the exercise or who understands the reason for Grenadian students having to travel so far. There is no question, of course, of reciprocal arrangements being offered to British students in Grenada, and so there is no parallel with the cultural student *exchanges* that are a valuable part of our own students' experience.

What are NHS patients gaining, either financially or in any other way, for this unnecessary invasion of their privacy? They see little obvious benefit if anything of the measly 25% of Grenadian students' fees that accompany them to Britain. Even Mrs Thatcher would surely regard this bit of private enterprise as a very bad deal.

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SIR,—Dr Smith's article (24 July, p 276) concerning St George's University School of Medicine, Grenada, was of particular interest to me. In February this year I was a visiting professor to the medical school, and offered a course to the medical students—an introduction to gynaecology. I received my medical education at the University of Sheffield in England, and qualified MB, ChB. Subsequently, I emigrated to the USA where I did postgraduate training in obstetrics and gynaecology at the University of Chicago, and have been involved in the practice of obstetrics and gynaecology and in teaching at the Medical College of Wisconsin in Milwaukee, USA. My observations may be of interest to you.

The quality of training of the St George's students is extremely high. They are, as Dr Smith observed, fluent in English, extremely highly motivated, and serious about their medical studies. The results of examinations which I conducted compared very favourably with American medical students. My impression is that when these young men and women qualify and enter medical practice they will be equal to their American contemporaries.

The clinical teaching facilities, certainly on the Island of St Vincent where I resided, were primitive and inadequate for bedside teaching. The students, however, receive their clinical training in accredited hospitals, mostly in the USA and a few in the UK.

Foreign medical graduates fill a vital role, certainly in the USA where the numbers of American graduates from medical schools do not adequately cover the needs of the nation. If government cannot supply this need but the private sector can and make a profit, why object? Medical schools which graduate well-trained English-speaking doctors in whom communicative skills are paramount, should be encouraged.

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Paraquat ingestion with methaemoglobinaemia treated with methylene blue

SIR,—I was interested to read the experience by Dr L L Ng and others (15 May, p 1445) with the treatment of methaemoglobinaemia as a result of paraquat ingestion, in which they suggested that cyanosis within hours of ingestion of paraquat should lead to the suspicion of methaemoglobinaemia and treatment with methylene blue.

As the authors have suggested, I also find it difficult to attribute the signs and symptoms to methaemoglobinaemia. Specifically, the degrees of cyanosis, symptoms, and the colour of the arterial blood attributed to methaemoglobinaemia do not correlate with the methaemoglobin value of 18·7%. Therefore, at first sight it is surprising that the institution of methylene blue had such a dramatic effect.

In occupationally exposed individuals the use of methylene blue for the treatment of mild to moderate methaemoglobinaemia tends to be withheld, initially, probably as a result of its paradoxic methaemoglobinaemia-generating activity, which is prominent in lysates.[1] As a result it has been practice to start methylene blue only if the methaemoglobin concentration exceeds 30% or if recovery is excessively slow.[2] In general, patients with acquired methaemoglobinaemia tolerate concentrations of methaemoglobin up to 20% without ill effect. At levels of 20% to 50% fatigue, weakness, dyspnoea, tachycardia, headaches, and dizziness may occur. Lethargy and stupor may appear with concentrations above 55%.[3]

All methaemoglobin-generating chemicals have additional toxic effects, and these side effects may make profound contributions to the toxic syndrome. In fact it is doubtful if any chemical agent induces an otherwise uncomplicated methaemoglobinaemia. Therefore it is probably inappropriate and misleading to suggest that there is a lethal concentration of methaemoglobinaemia without taking account of the particular agent.[4] Despite the latter consideration it is generally agreed that a reduction in the circulating titre of abnormal pigment is a desirable therapeutic goal. If the methaemoglobinaemia is contained within intact and functioning erythrocytes the methylene blue certainly evokes a dramatic response.[5]

In light of the interesting experience of the authors, and accepting the concentration of methaemoglobin before treatment, one wonders whether electron carriers such as methylene blue have, in addition to their anti-methaemoglobinaemia function, a therapeutic role in the treatment of the other toxic effects observed with such compounds. If, in the deactivation of the other metabolites associated with similar toxic substances, pathways such as the dormant reduced nicotinamide adenine dinucleotide phosphate system are involved then it is not unreasonable to assume that the electron carrier methylene blue would have a beneficial effect. The identification of such pathways, if they in fact exist, are matters for future toxicological research.

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Immune guided missiles

SIR,—In the recent leading article (14 August, p 461) on the use or serotherapy it was stated that no immune response to the foreign protein in monoclonal antibodies occurs. This unfortunately is not always the case. Cosimi *et al*,[1] using a murine anti-T cell antibody for the reversal of kidney rejection after transplantation, detected high concentrations of anti-mouse immunoglobulin antibodies, which prevented administration of further courses. Miller *et al*[2] reported similar findings in a patient with T-cell leukaemia although in their patient the effect of the anti-mouse antibody was clinically insignificant.

We have recently treated a patient with a low-grade T-cell proliferation using a murine hybridoma monoclonal antibody which was administered on repeated occasions.[3] Within 26 days the development of anti-mouse antibody, detectable at a serum dilution of 1/1250, totally inhibited the effect of further serotherapy.

Small doses of aggregate-free heterologous immunoglobulin may be tolerogenic in animals,[4] but this may not be the case in humans. In addition the immunosuppressive effects of the underlying disease or concurrent therapy may not be sufficient to depress the patient's humoral immune response.

Although the patients developing these anti-mouse antibodies have not suffered overt immune-complex disease, further treatment is usually prevented, and this may be a serious limiting factor in the development of mouse monoclonal antibodies for widespread use. This factor should be considered in planning treatment with these antibodies. Ideally they should be given only in short courses, or additional therapy should be given to reduce sensitisation to the foreign protein. In our patient and in the patient of Miller *et al* no additional chemotherapy was given and in the treatment of transplant rejection the administration of monoclonal antibody was used in some of the patients to allow reduction in the immunosuppressive agents. This may have

contributed to the development of anti-mouse antibody.

The development of human-derived monoclonal antibodies may prevent or at least minimise this problem in the future.

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[1] Cosimi AB, Calvin R, Burton RL, *et al. N Engl J Med* 1981;**305**:308-14.
[2] Miller RA, Maloney DG, McKillop J, Levy R. *Blood* 1981;**58**:78-86.
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Obstructive sleep apnoea syndrome

SIR,—In your leading article on obstructive sleep apnoea syndrome (21 August, p 528) Dr J R Stradling made no reference to mandibular size when discussing the possible aetiological factors involved. During the past two years, I have seen three small boys who had experienced numerous episodes of obstructive sleep apnoea. In each case the mandible was abnormally small.

The first patient, aged two years, had an asymmetrical micrognathia due to ankylosis of the left temporamandibular joint. The ankylosis was excised, and the joint was reconstructed using a costochondral graft. Eighteen months later there is good manidbular opening, facial growth appears to be proceeding normally, and there have been no further apnoeic attacks.

The second patient was five years old, and had Treacher Collins syndrome. Surgical rotation and advancement of the very small mandible has resulted in an improved facial profile and the cessation of episodes of nocturnal apnoea.

The most recent patient, aged two, exhibited the features of bilateral hemifacial microsomia. Persistent obstructive sleep apnoea had necessitated a tracheostomy at the age of three months. Mandibular reconstruction six months ago has improved the appearance, but it has not been possible to remove the tracheostomy tube. This is probably due to an element of pharyngeal hypoplasia, an occasional feature of hemifacial microsomia.[1]

Recognition of micrognathia as a cause of obstructive sleep apnoea, and appropriate surgical correction, may obviate the need for a long-term tracheostomy.

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[1] Shprintzen RJ, Croft CB, Berkman MD, Rakoff SJ. *Cleft Palate J* 1980;**17**:132-7.

SIR,—I found your leading article by Dr John R Stradling (21 August, p 528) both interesting and educative. I would like to bring to the attention of your readers another cause of the syndrome and its management.

Kuo *et al*[1] reported in 1979 three patients who were suffering from the syndrome, and the next year Bear and Priest[2] reported another case. All four patients suffered from retruded mandibles. The management in all four cases was by a pull-forward mandibular osteotomy. This increased the pharyngeal air space and allowed normal sleep pattern. This operation prevented a permanent tracheostomy with all its disadvantages.

Recently I have been involved in the management of a girl with the syndrome who has benefited from a bimaxillary pull-forward osteotomy. She was born with a Pierre Robin syndrome but did not develop the sleep apnoea syndrome till she was 16 years of age. Early postoperative results have been good, but there is always the danger of relapse, hence the long-term results of the treatment are not yet available. Bimaxillary osteotomies allow patients with normal dental occlusion to benefit from the advantages of mandibular pull forward but still retain a normal dental occlusion.

Patients who have the syndrome might benefit if oral surgeons are added to the team who are involved in the management of these patients. Not only is the syndrome helped with an osteotomy but the patient might also benefit from an improved facial appearance, an improved dental occlusion, or both.

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[1] Kuo PC, West RA, Bloomquist DS, McNeil RW. *Oral Surg* 1979;**48**:385-92.
[2] Bear SE, Priest JH. *J Oral Surg* 1980;**38**:543-9.

Problems with perinatal pathology

SIR,—Like Dr H Kohler (5 June, p 1709), I also applaud the efforts of Dr A J Barson and others (27 March, p 973) in highlighting the serious lack of paediatric pathologists.

It may seem strange for a psychiatrist to enter this debate to plead for more (and better trained) paediatric pathologists, but in my work with bereaved families following the loss of a baby from "cot death" or sudden infant death syndrome I share the view of my paediatric and other colleagues that this diagnosis at a coroner's necropsy (usually totally appropriate in the circumstances as I have explained elsewhere[1]) depends entirely on the sophistication and expertise of the pathologist involved.

The definition, of course, of a sudden infant death turns on the event occurring in an apparently healthy baby. Professor John Emery[2] and others over the past few years have explained how a detailed necropsy may, in the hands of an experienced paediatric pathologist, reveal abnormalities in some of these hitherto unexplained deaths. For a proportion of parents, therefore, there may be a pathological explanation which may help them to bear the loss of their child and help those supporting them to relieve the guilt and self-blame which they so commonly experience.

Even where no clear pathological evidence of disease is forthcoming, we are aware that it is extremely helpful and constructive for the parents to know that the investigation was carried out in detail by a pathologist with training and experience in the field.

It would be wrong, however, to suppose that only these parents of babies dying of sudden infant death syndrome experience bewilderment and confusion following the death of their baby. Others with whom I have been involved clinically (including a study of 100 families following infant deaths) are parents whose baby has been stillborn or has died in the neonatal period. Both from the very important point of genetic counselling made by Dr Kohler and that of bereavement counselling and support, adequate information as to the cause of death and likelihood of recurrence are vital.

It is now widely understood and accepted that physical, psychiatric, and psychosocial sequelae following bereavement do occur and that preventive intervention is important and effective.[3] The prevention and mitigation of family distress and marital pathology is surely a worthwhile objective, and in this context any improvement in the quality of necropsy information available is most desirable.

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[1] Bluglass K. *J Child Psychol Psychiatry* 1981;**22**:411-21.
[2] Emery JL, McWeeney P. *Arch Dis Child* 1975;**50**:191-96.
[3] Parkes CM. *Br Med J* 1980;**281**:3-6.

A resurgent evil

SIR,—I agree with all of Dr J P Lester's principles (21 August, p 548) except the one advocating parity in three years. Maximum earnings at about age 30 years, in only the fourth year of a career of about 38 years, is quite imbalanced and unlike the conditions obtaining in any other profession.

I would advocate a much longer "incremental" scale starting at 60% of the maximum and rising by 16 steps of 2½% annually to reach parity. Extra increments would be awarded for postgraduate experience additional to vocational training, one increment for each year, and for postgraduate degrees and diplomas. One extra increment might be appropriate for the diploma in child health while membership of the Royal College of General Practitioners would command five. (All partners with membership of the Royal College of General Practitioners should also take the multiple choice questionnaire paper every five years and would lose five increments (12½%) on failure. The college should make provision for such multiple choice questionnaire only tests.)

Thus the applicant who qualified at 24 and has done vocational training, passed the diploma in child health and membership of the Royal College of General Practitioners, and eventually joins a practice at 34 would start with 12 increments (90%) and reach parity in four years; the vocationally trained but without further qualifications or experience would have 16 years to parity (reduced by five as soon as he passes membership of the Royal College of General Practitioners).

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SIR,—I was pleased to read Dr J P Lester's article "A resurgent evil" (21 August, p 548). The fact that it was written by a course organiser was very encouraging as it would appear that the importance of the "business" of general practice is now being more widely taught. The GMSC is aware of problems in this field, and the report of a working party is awaited. In Scotland for many years the SGMSC has published advice on partnership agreements and offered an advisory service on proposed agreements submitted to it. This has proved valuable for the whole profession in