With cryptogenic disease it is impossible to be certain of the prognosis for these infants if they had not had surgery, but such deaths are exceptional and some component of the laparotomy or cholangiography may have contributed. These infants avoided a more immediate hazard of laparotomy—namely, in those with severe liver disease and markedly reduced bile flow, the removal of narrow but patent bile ducts because of a mistaken diagnosis of biliary atresia.⁷

Further, Thaler and Gellis⁸ have shown that infants with hepatitis submitted to laparotomy and operative cholangiography are more likely to develop cirrhosis than those with a condition of similar severity who are spared these investigations. I therefore submit that laparotomy and operative cholangiography are not simple procedures in infants with hepatobiliary disease and can safely be avoided in the vast majority. It would be a pity if the improved survival with a good quality of life for some infants with extrahepatic biliary atresia were to be counteracted by unnecessary morbidity and mortality from laparotomies in infants with hepatitis.

While the lure of "new and exotic liver function tests" may contribute to the delay in surgical treatment, more important factors appear to be the failure of parents, health visitors, and some family doctors to appreciate that hyperbilirubinaemia with dark urine is always pathological and requires investigation, and persisting and understandable doubts among some paediatricians about the long-term prognosis in biliary atresia even if satisfactory bile drainage is achieved following portoenterostomy.

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³ Mowat, A P, Psacharopoulos, H T, and Williams, R, *Archives of Disease in Childhood*, 1976, **51**, 763.

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⁵ Howard, E R, and Mowat, A P, *Archives of Disease in Childhood*, 1977, **52**, 825.

⁶ Porter, C A, et al, *British Medical Journal*, 1972, **3**, 435.

⁷ Witzelben, C L, *Proceedings of an International Workshop on Neonatal Hepatitis and Biliary Atresia*, Washington DC, 1977, in press.

⁸ Thaler, M M, and Gellis, S S, *American Journal of Disease in Childhood*, 1968, **116**, 257.

Dangerous antihypertensive treatment

SIR,—We feel that a note of caution should be sounded about the introduction of combined tablets of beta-blocking agents with a diuretic in the treatment of hypertension. Both beta-blocking agents and diuretics given alone can be potent hypotensive agents. Oxprenolol and other similar agents may lower the systolic pressure by as much as 60 mm Hg¹ and thiazide diuretics are capable occasionally of producing similar large falls. It seems clear that when the two agents are used together their effect is simply additive.

Your recent leading article (28 July, p 228) on dangerous hypotensive therapy has correctly drawn attention to the dangers of lowering blood pressure too rapidly. One of the patients reported by Dr D H Cove *et al* (p 245) lost vision when treated by mouth with methyldopa, to which propranolol and later a diuretic were added. Their blood pressure chart shows the systolic pressure falling from

almost 300 mm Hg down to 150 mm Hg in 12 hours and to 100 mm Hg on the second day. It was at this time that the patient was found to be blind. Our own experience supports the conclusion that rapid reduction of raised blood pressure, particularly by the intravenous route, may be dangerous and we have certainly witnessed cerebral infarction occurring within a few days after beginning hypotensive therapy by mouth. This has led us to speculate over the relationship between pressure reduction and cerebral events.

In our view therefore it is correct to use either a beta-blocking agent or a diuretic in the first place and if the second agent needs to be added then it is eminently sensible to give the two agents in one tablet. This minimises the number of tablets to be taken. The tablets can be presented in calendar packs to aid the patient's compliance and the majority of hypertensives will probably not then need more than one tablet each day. Both beta-blocking agents and diuretics have a very flat dose-response curve^{2,3} and in most combined preparations the doses contained in the tablet are at the top of this curve. Apart from the risk of inducing complications from rapid lowering of blood pressure, the use of two agents when one might suffice doubles the chance of producing unwanted side effects. With beta-blockade either airways obstruction or cold extremities may be unnecessarily produced. If beta-blockade alone suffices to lower pressure then it is bad medicine to introduce the further risk of producing hypokalaemia, gout, or diabetes with a diuretic.

Promotion of the combined tablets should be preceded by the advice that either a beta-blocking agent or a diuretic should be used alone in the first place and the combination is only indicated if a second agent is really necessary.

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¹ Marshall, A J, Barritt, D W, and Harry, J D, *Postgraduate Medical Journal*, 1977, **53**, suppl No 3, p 168.

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Rebound effect after stopping beta-blockers

SIR,—Dr T J B Maling and Professor C T Dollery (11 August, p 366), describing four patients followed for four days after stopping propranolol, observed no rebound increase in supine or erect blood pressure or heart rate, so adding more apparently reassuring evidence to counter the anecdotal alarms about the dangers of propranolol withdrawal. We feel we should draw attention to data^{1,2} which clearly show that a rebound increase in adrenergic activity does occur after stopping propranolol. Our more recent findings (unpublished) indicate that the phenomenon occurs also after treatment with other beta-blockers, particularly those that lack intrinsic sympathomimetic activity. As might be expected, the manifestations of this presumed increase in beta-receptor "sensitivity"³ become more pronounced under conditions of increased sympathetic drive.¹ We suggest that this is why the phenomenon has been missed in other formal studies of beta-blocker withdrawal and, equally but more importantly, why it may be dangerous when sympathetic

activity is high enough to override residual beta-blockade. Vasodilators, for example, will increase sympathetic activity, and the sympathetic stress of coronary artery surgery must be overwhelming. Catecholamines are a well-known experimental means of inducing myocardial necrosis indistinguishable from the changes of ischaemia.⁴

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¹ Ross, P J, et al, *Lancet*, 1979, **1**, 875.

² Nattel, S, et al, *Circulation*, 1979, **59**, 1158.

³ Glaubiger, G, and Lefkowitz, R J, *Biochemical and Biophysical Research Communications*, 1977, **78**, 720.

⁴ Rona, G, et al, *Archives of Pathology*, 1958, **67**, 443.

Short-term vocational medical work overseas

SIR,—Doctors who consider short-term work overseas (14 July, p 111) fall into two broad groups: those in hospital specialties, and those in general practice, public health, or the uncommitted stages of hospital practice. The major deterrent for most of the former is the near impossibility of regaining on return a place on any rung of their specialty ladder comparable to that which they left.

Most developing countries which ask for hospital doctors now require trained specialists; and, apart from the legal requirements of seniority, the unsupervised nature of the work and the extent and variety of clinical experience which many such posts present would place an intolerable burden on inexperienced shoulders. This means that most hospital doctors entering specialist work overseas will leave this country at consultant, senior registrar, or late registrar level. Consultants may be allowed prolonged leave of absence; senior registrar posts cannot usually be "held" for more than a year while the incumbent is abroad; and registrar posts must often be resigned completely.

Work overseas for a year or less at this level is of limited usefulness because of the problem of language and general familiarisation with the environment and the spectrum of disease. But those who resign their posts in these grades to serve for longer than a year face extreme difficulty in returning to their grades in the NHS, especially in major specialties, presumably because of doubts about the training content of largely unsupervised work.

The following suggestions might be considered in an attempt to resolve this impasse. (1) A small number of posts, decided on an individual basis, could be kept open for a longer period—say two years. (2) Each candidate should ensure, before signing any contract, that he acquires as much reliable information as possible about job content: newly created posts merit particularly close scrutiny. There should be much more collation of information from all potential overseas employers, together with "feedback" from past employees for circulation to postgraduate deans and others who may be called on to advise doctors—an "Overseas Yearbook" perhaps? (3) The establishment of a close link by the overseas doctor with a senior specialist in the UK in an advisory capacity would do much to maintain standards and morale. We envisage the advice being related to methods of collecting and recording clinical information and preparing material for possible publication; provision of references would also be an asset. (4) As a condition of retaining his UK post, the candidate should be required to produce regular and reasonably detailed reports on his work, perhaps to the joint higher training committee of his specialty. (5) It might be possible to arrange occasional inspection visits by, for example, UK

consultants if they were in that part of the world anyway. It amazed us to find how many "travelling experts" came within a few hundred miles of our remote mission hospital in Kurdistan. (6) For the few who for any reason (such as revolution) return after a longer period, the authorities might consider creating personal part-time supernumerary posts of limited duration. This would be infinitely preferable to a succession of locum posts, or prolonged period of unemployment, with no eligibility for state benefits because of previous absence from the UK, often on a salary too low to save capital or maintain UK National Insurance contributions.

Doctors who are more junior would be well advised to look for supervised posts—for example, in the universities of developing countries or in larger Christian hospitals with experienced senior staff, so that responsible reports of their work would be provided. At this stage a shorter period of a year or so could be useful to the overseas community.

Finally, those individuals who work in developing countries may have something worth while to offer the NHS on return. They value highly the privileges of working in our NHS. In addition to their extensive clinical experience, they have experience in decision making and responsibility under difficult circumstances which may give them a more mature viewpoint in consultant practice; there should be scope for those who have gained a broader experience of medicine from contact with different spectra of diseases and alternative schemes of health care. Since no "ideal" training for consultant practice has yet been devised or identified, these points provide a valid argument at least for considering such work for retrospective recognition by joint higher training committees.

Those who choose to work in developing countries are likely to have a high sense of vocation in their careers, and, although expecting no preferential treatment, they should not be penalised. They have in fact much to contribute to the NHS, which was after all conceived as a service to the community.

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Mission hospital medicine

SIR,—Following Dr Anne Savage's article (14 July, p 111) there have been a number of letters expressing interest in medical missions and the desire for an office of information of such opportunities abroad (4 August, p 335 and 11 August, p 388). Both the Medical Missionary Association and the Christian Medical Fellowship have for years provided such advice, the former through their quarterly magazine *Saving Health*, which includes an analysis of advertised needs of the many British missionary agencies. The CMF maintains individual correspondence and liaison with Christian medical associations of the Third World through which (and including missionary and government agencies) over 300 members of the CMF are currently serving. Also, Dr Peter Green of the MMA is the official BMA representative for British missionaries.

We would be happy to advise any who want to help overseas missions. Varied opportunities and needs abound. However, it should be noted that most mission hospitals request expatriates who are at least in sympathy with the ideals of serving in the name and spirit of Jesus Christ, the significance of which is not readily apparent in privileged Britain. We would gently, modestly, and in all sincerity plead for expatriates to "give up" (you won't,

you'll gain!) a few years or make an open-ended commitment to serve abroad, and to go not primarily seeking "interest" or "experience" but to understand the real needs of the situation and adapt oneself to meeting those needs. Besides, there is a growing resentment in the Third World against those whose contribution is so obviously geared to personal ambition or specialty. As one national superintendent put it, "Let them make such mistakes on their own people before they practise on us."

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SIR,—My experience of mission hospital medicine was in a hospital specialising in eye surgery in the Bihar area of North India and my lasting impression is of the tremendous amount of high quality work that was done with the minimum of staff and equipment. The experience has also made me, like Dr C J Burns-Cox (11 August, p 388), critical of the waste and pomposity prevalent in the NHS and I am sure that a spell doing clinical medicine or surgery in a poor country would be of value for anybody intending to work in clinical medicine, though it might be of even greater value for potential community medicine specialists.

In contrast to the BTU (been to an underdeveloped area), the BTA (been to North America) has always been considered to be an advantage to a career in the NHS. Nevertheless, the fear of losing a place on the NHS career ladder meant that no senior registrar from my teaching hospital was interested in following me for a year as staff anaesthetist in a Toronto teaching hospital. Dr C J Chandler (p 389) should therefore not be too surprised at the lack of interest in the BTAf.

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SIR,—The two recent letters by Drs C J Burns-Cox and C J Chandler (11 August, p 388) on mission hospital medicine reinforced the call by Dr Anne Savage (14 July, p 111) for a central register both to refill vacated Third-world posts and to find the returning doctor a rung on the ladder back home.

Neither mentions one other very important function of such a registry. It must have up-to-date information on the political and economic climate of the country involved. Although few doctors are likely to go to Uganda at the present time, there was a time when Makerere University was a hive of research for adventurous registrars, and let us hope it will be again. About three years ago I asked a BMA spokesman about the advisability of going to a particular Third-world country. Although it was a well-known area, he could neither tell me anything positive nor put me in touch with any doctor who had recently been there. All he could say was, "Australia and Canada are always a safe bet." Now, only three years later, both those countries are overdoctored.

It is a sad fact that there was never a time when Schweitzerian philosophy and medicine were more apt than now, and never a time

when they were less likely to be carried out. The "wind of change" has become a tornado, and let no doctor think he is immune. Such a registry therefore must have realistic information about the country or State to which it is recommending the enthusiastic doctor. If it does not, rather than graduate BTAf, he may join the even more distinguished band of NHS (never heard of since) doctors.

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Clioquinol and related drugs

SIR,—All of us were foreign (that is, non-Japanese) participants in the International Conference Against Drug-Induced Sufferings, held in Kyoto 13-18 April 1979. We find the evidence overwhelming that medicines containing certain hydroxyquinoline compounds, such as clioquinol, can cause serious and irreversible injury to the nervous system. We urge those manufacturers who are still selling these products either to provide clear evidence that there are benefits which justify the risks or to withdraw them. In our opinion, the reassessment of these drugs is an urgent task for national drug regulatory authorities and international organisations.

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Metronidazole in the aetiology of pseudomembranous colitis

SIR,—It has been suggested that metronidazole alone may be implicated in the aetiology of antibiotic-associated pseudomembranous colitis following the report by Dr A Kappas and others (18 March 1978, p 675) that a single patient developed pseudomembranous colitis after having metronidazole. As metronidazole alone has little influence on faecal microflora we questioned whether this patient received any other antibacterial agents. A detailed study of the notes revealed that the patient was given lincomycin in addition. The prescription sheet was missing from the notes and the information that this person received lincomycin became evident only as a result of careful scrutiny of the nursing records.

We apologise for this error and we would emphasise that the paper in question was concerned with the diagnosis of pseudomembranous colitis and not with a detailed investigation of its aetiology. We feel that it is most important to point out this error since we know of no patient reported so far in the