Transkei, any travel agent will advise on flights to Johannesburg and their cost. Some of the lesser-known flights—for example, Luxavia—are good value, or it might be worth becoming, for instance, a Friend of the Springboks for their charter flights. If there's time, the sea voyage is enjoyable. Rail or coach or both take you on to Umtata.

Pros and cons

If you're thinking seriously of a short time in a developing country, you would probably enjoy this sort of job. Patients get better, and seem to enjoy doing so, so it is immensely rewarding in terms of job satisfaction. There is excellent clinical experience to be had, and the chance to become clinically more self-reliant. The medicine, however, is probably relatively elementary, and facilities for definitive investigation are limited. Also, demand on scarce medical resources is enormous—at times the resources seem so thinly spread as to be depressingly ineffective. Rural hospitals are very isolated, and doctors and their families are thrown very much on their own social resources. There are all the disadvantages of leaving the NHS for a while, in terms of superannuation, salary increments, and so on, and the posts are not officially recognised by the Royal Colleges as suitable for vocational training experience. Many will not like the political climate of Southern Africa, although Transkei's paramount chief promises a "non-racial society in which race, creed, or colour will not be the criteria of a man's worth." This has certainly been the philosophy of the mission hospitals throughout their history.

Transkei has immense potential. It is a land of stark contrasts —wealth and poverty, health and disease, wisdom and ignorance. I marvelled as one evening a white-gloved waiter served wine at a dinner party under the chandeliers of Umtata's Imperial Hotel —four hours and 40 miles away I had been among the flies and smells of a ramshackle mud hut in the bush examining a marasmic infant, poisoned by a witch doctor's herbal medicine. Worlds apart, but perhaps the gulfs that divide them are gradually closing.

Doctors wishing to work in Transkei should apply to the Secretary for Health, Department of Health, Private Bag, Umtata 5100, Transkei. Further information before applying may be had from Dr Guy Daynes CBE, Umzimkulu Hospital, Private Bag 514, Umzimkulu 4660, Transkei, whose help I gratefully acknowledge.

For Debate . . .

Monitoring adverse reactions to drugs

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The number of patients and the duration of treatment that can be included in controlled clinical trials before a drug is marketed make it impracticable to detect any save the most common adverse effects of drugs. To minimise the hazard of toxic effects under conditions of general use some kind of monitoring and early warning system is needed. In Britain the Committee on Safety of Medicines (CSM) pioneered the use of a voluntary system of spontaneous reporting by doctors on prepaid addressed postcards (yellow cards). These cards have proved valuable in several investigations when adverse reactions were known or suspected, but they are of little use in relation to their main purpose: the detection of previously unrecognised adverse drug effects. Moreover, they give no indication of the incidence of adverse reactions. Those who use yellow cards mainly report toxic effects that are already known.

The deficiencies of the yellow-card system are highlighted by their failure to detect the serious toxicity to eye and peritoneum caused by the beta-receptor-blocking drug practolol. It was only after Mr Peter Wright, an ophthalmic surgeon at Moorfields Eye Hospital, published his findings that large numbers of reports of damage to the eye caused by practolol were made to the CSM. A different type of monitoring system is therefore required: one that achieves a higher reporting rate and identifies previously unknown reactions and estimates their incidence. An arrangement of this sort is often referred to as monitored release.

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Monitored release

The basic concept of monitored release is that the pharmaceutical company marketing a new drug should have a duty to obtain reports on all patients treated up to an agreed number. In early experiments using this idea the individual companies were left to devise their own methods of collecting information. They found great difficulties in persuading doctors to complete report forms, and the information obtained was of limited value. The problem became even worse when the promotional side of some leading pharmaceutical companies debased the concept of monitored release to something that resembled buying prescriptions. Doctors were promised new stethoscopes, medical bags, calculators, etc in return for completing "report forms." These forms did not seem to be seriously intended for monitoring drug toxicity, and the whole exercise fell into the category known in the industry as a "promotional trial."

The concept of positive monitoring is so important that it cannot be allowed to slide into ignominy in this way. Our proposals are designed to overcome some objections to existing schemes and to ensure that data are collected in a valid and usable manner.

Registered release

Any practical scheme of monitoring necessarily involves a stage of patient registration in a form that can be retrieved without ambiguity about the identity of the patient and the drug. The willing co-operation of doctors is an essential component, and to achieve this two main demands must be met: payment for the additional work load, and maintenance of confidentiality of clinical information. Our scheme would begin by placing a duty on the pharmaceutical company to complete a quota of registrations for a new drug before it went on free sale. The NHS would pay for these prescriptions in the ordinary way, but the company would not be able to promote the drug for general use until the quota had been reached. If an attempt was made to circumvent this arrangement it might be necessary to take powers to prevent prescriptions being dispensed for unmonitored patients, or for the NHS to decline to pay for any prescriptions other than those for monitored patients until the quota had been filled. The quota might be 5000-10 000 for a commonly used drug, tens or hundreds for one designed to treat less common conditions.

The registration documents could be distributed to doctors by pharmaceutical company representatives or by district and area pharmaceutical officers. Although we would prefer the latter arrangement, the practicalities probably dictate that the existing company representatives would have to be used. Patients who were to be prescribed a drug on registered release would be told that this was the case and asked if they would agree to complete a questionnaire at intervals concerning their experience with the drug. Registration would be accomplished by the doctor completing a simple four-part no-carbon-required document. The top copy would have a serial number; the drug name; the date and dose prescribed; the diagnosis; the patient's National Health Service number; the name, address, sex, and date of birth of the patient; and the name and address of the registering doctor. This copy would go into the doctor's notes. The next copy, containing the same information, would go to the registering agency (see below). The third copy would go to the Office of Population Censuses and Surveys (OPCS). The fourth copy, which would contain only the serial number, the drug name, and the NHS number of the patient, would go to the pharmaceutical company. This would provide them with evidence that they had filled their quota, which they would present to the licensing authority to receive a certificate of free sale.

Follow-up

The doctor who had registered the patient would have no special responsibility until he received a questionnaire from the registering agency, but he would be encouraged to use the yellow-card system if he noticed anything unusual.

The agency would be charged with registering the patients on a computer-based file and at intervals sending out a questionnaire to the patient and the doctor. Once a year for five years might be suitable spacing for many new drugs, but it could be varied for other requirements. The questionnaire to the doctor would ask whether the patient was still on the drug and about all diagnoses or hospital referrals made during the previous year. Completion would attract a small fee. The patient would receive a much more detailed questionnaire. It would cover the same ground as the questionnaire to the doctor but would include a battery of questions about many different bodily systems and symptoms. The questions could be varied depending on the properties and use of the drug. Experience has shown that an 80% response rate can be obtained to symptom questionnaires sent to patients with one reminder.

The symptom questionnaires would be subjected to computer analysis looking for unexpected patterns or grouping of untoward events. In return for a tagging fee, the OPCS would be asked to report all deaths in the monitored group for up to 20 years thereafter. This would ensure that deaths would not be overlooked simply because the patient had moved house or the use of the drug had been forgotten. The scheme should be invaluable for evaluating the risk of carcinogenesis or increase in the incidence of a known disease with a fatal outcome, such as myocardial infarction.

Confidentiality would be maintained because the pharmaceutical company would not know the name and address of the patient, but in an emergency, with the aid and authority of the NHS, it could decode the NHS number on their monitoring file.

Costs and fees

Such a system would not be cheap to operate but could be regarded as a reasonable charge on drug development costs in return for the possibility of relatively early marketing of a new product. The CSM would determine whether a new product had to be registered, how many patients had to take it, and for how long. New chemical entities would always be registered. The cost of the scheme would fall on the sponsoring pharmaceutical company. The fees to the doctors (we suggest £2·50 for the initial registration and £1·00 for the follow-up) would be paid via the registration agency. A patient registered for one product could not normally be registered for another until five years had passed.

The registering agency

The registering agency could be the pharmaceutical company, the CSM, or another body such as the Royal College of General Practitioners or the Royal College of Physicians. There are advantages and disadvantages in each possibility. The pharmaceutical company has the greatest concern with the outcome and the resources to do it well, but some companies have been suspected of dragging their feet in reporting adverse reactions, especially when these reports are unconfirmed. Safeguards about prompt disclosure and confidentiality would be needed if the company were to undertake the work. The CSM might in many ways be the best body to undertake this work as it is impartial and would have an interest in running an efficient system. Some doctors have reservations about disclosing information to a government agency, however, and a separate body administered by a professional group, such as one of the royal colleges, might have advantages. The problem would be to assemble sufficient expertise and to cope with the administrative load. The choice among these three options would require discussion among the interested parties.

We believe that a system of this sort would work, and propose that it might be tried with some of the newly marketed and about-to-be-marketed beta-receptor-blocking drugs for which the possibility of a practolol-like adverse reaction cannot yet be denied.

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ONE HUNDRED YEARS AGO Recently, in noticing the illness of Prince Adolphus of Teck, we mentioned that another sample of water from Sidmouth Spring in Richmond Park was to be forwarded by Dr Wadd to Professor Frankland for analysis. It was duly sent, with the result that no cause for the typhoid fever of Prince Adolphus was discovered therein. Nor can anything wrong be so far found with the drainage of White Lodge. Her Royal Highness Princess Mary of Teck has consequently been advised to apply to the Metropolitan Board of Works or to the Privy Council, to have the sanitary condition of the Lodge thoroughly examined. The other children of Her Royal Highness were sent from White Lodge to Kensington when Prince Adolphus was taken ill; and we hear that Prince George of Teck has since had a feverish attack, with diarrhoea. (*British Medical Journal*, 1877.)