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HTLV-I infection in British and Jamaican relatives of British patients with tropical spastic paraparesis

SIR,—The results of the study by Dr J K Cruickshank and colleagues on the seroprevalence of human T cell leukaemia lymphoma virus type I (HTLV-I) in the families of 11 Jamaican immigrants with tropical spastic paraparesis in London¹ differ from our results in the west midlands.² In our study most, though not all, of the available United Kingdom resident members of the families of seven patients with tropical spastic paraparesis agreed to testing for HTLV-I antibodies. All of the patients were women—six from Jamaica and one from Saint Vincent. Their HTLV-I state was established by using passive particle agglutination, enzyme linked immunosorbent assay (ELISA), and immunofluorescence tests.² All three husbands tested positive; one of them had adult T cell leukaemia lymphoma. Of five Jamaican born children, one tested positive.

Whereas Dr Cruickshank and colleagues did not find any of 14 children born in the United Kingdom to be seropositive, two out of 10 children born in the United Kingdom whom we tested were seropositive. They were both the daughters of a woman with tropical spastic paraparesis (onset 1980) and a man with adult T cell leukaemia lymphoma (onset 1986). One was aged 28 and had visited Jamaica for a few months when aged 13 and 25; the other was aged 21 and had never visited the West Indies. They had two seronegative younger brothers who were born in the United Kingdom and were living in the west midlands and one seropositive older sister who was born in Jamaica. Two other brothers and two other sisters who were born and resident in Jamaica were not tested. All of the children in our family study (except one seronegative son) were breast fed, and none of the seropositive relatives had received a blood transfusion.

The fact that the two daughters who were born in the United Kingdom were positive for HTLV-I antibody indicates that children of Jamaican immigrants with tropical spastic paraparesis may seroconvert in this country, not just in the West Indies. When the data for United Kingdom resident children of patients with tropical spastic paraparesis in the west midlands and London are combined five out of 14 (36%) Jamaican born children and two out of 24 (8%) United Kingdom born children were seropositive; this difference is not significant (Fisher's exact test). Although maternal transmission may not be the only route of infection in these children, these results do not support the arguments of Dr Cruickshank and colleagues against maternal transmission as the main route. The numbers in both the London and west midlands studies are small, but further testing of the available families of patients with tropical spastic paraparesis or adult T cell leukaemia lymphoma may provide an explanation for familial clustering of HTLV-I infection.

Dr Cruickshank and colleagues state that there

are no available and adequate data on HTLV-I seroprevalence in Jamaican born immigrants in Britain except their own (unpublished) study of 81 Afro-Caribbean subjects in London, in whom they found an HTLV-I seroprevalence of 2.5%. We have carried out anonymous testing for HTLV-I antibody in Afro-Caribbeans in the west midlands and found that seven out of 192 (4%) of West Indian born subjects were seropositive, but none of 403 United Kingdom born subjects of Afro-Caribbean origin were seropositive. Despite different study methods the seroprevalences in the west midlands and London groups of West Indian immigrants were not significantly different (Fisher's exact test) and are comparable with the seroprevalences reported in Jamaica.³ The difference in seroprevalence between the United Kingdom born and immigrant Afro-Caribbeans in our study is significant (χ^2 test, $p < 0.001$), but this difference has not been found in the family studies.

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- 1 Cruickshank JK, Richardson JH, Morgan OStC, et al. Screening for prolonged incubation of HTLV-I infection in British and Jamaican relatives of British patients with tropical spastic paraparesis. *Br Med J* 1990;300:300-4. (3 February.)
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Housing and health

SIR,—I would like to congratulate Stella Lowry on her thoughtful articles on housing and health.¹ May I put in a plea, however, for doctors to keep a foot in both camps—in the real if chaotic role of helping to prioritise housing applicants and as white knights crusading for decent housing.

I agree that in most cases a doctor's opinion is superfluous, and as stated in the article a medical degree is not required to spot the most needy cases. It can be helpful, however, in deciding whether a disability is permanent and stable, curable over time, or progressive.

Another reason for pleading for the continued involvement of a doctor is that over the years requests for rehousing have provided a fruitful source of case finding for young and elderly handicapped people, who have either not contacted or not been helped by the statutory services. These include those with deteriorating multiple sclerosis, people with multiple diseases living in sub-standard housing, travellers with handicapped children, and so on.

Incidentally, the new district public health annual reports are a heaven sent platform for campaigning for decent, affordable housing and for illustrating the deteriorating position vis à vis its provision.

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- 1 Lowry S. Housing and health: housing for people with special needs. *Br Med J* 1990;300:321-3. (3 February.)

Cancer of the oesophagus

SIR,—Dr I C M Paterson¹ accuses Mr John Bancewicz² of being unbalanced in his article on cancer of the oesophagus and then proceeds himself to offer a most unbalanced view on the subject. The gist of his letter is that surgery has no

advantage over radiotherapy, and he quotes the reviews by Earlam and Cunha-Melo.^{3,4} In fact one of these critical reviews of surgery¹ reported a 12% and not a 4% survival at five years. In patients leaving hospital the five year survival went up to 18%. On the other hand the review of radiotherapy showed a five year survival of 6%.⁴ These figures are in line with those in most published work. Maybe this would explain why Earlam's prospective trial between surgery and radiotherapy⁵ failed because of inadequate recruitment, as Dr B S Mantell complained in his letter.⁶

Of course surgery can be offered only to a selected group of patients, and this has been fully recognised by us.⁷ Surgery, however, gives such patients the best chance of prolonged survival. If surgery is done in a specialised unit with a low mortality and short stay in hospital then Dr Paterson need not worry too much about its cost effectiveness. Radiotherapy may be cheaper, but the patient's interest is paramount.

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Stone fish bite

SIR,—Other readers have drawn your attention to the fact that the injury produced by a stone fish is caused by the highly venomous spines^{1,2} and not a bite as suggested.³

The stone fish is extremely hard to see in the natural environment, and practically all stings reported occur on the feet or hands. In an isolated area the extreme pain and distress plus impending local tissue damage can be difficult to manage, especially in the absence of antivenom. The only stone fish antivenom available is produced by our laboratories. We receive many reports of its use and have no reason to doubt its effectiveness when given promptly with other recommended management.⁴

Advice on first aid and treatment has been under constant scrutiny for some years. We believe that the current protocols are rational and minimise injury to the patient. These protocols are modified depending on the type of venomous organism concerned. With a stone fish sting we agree that appreciable pain relief is often obtained by bathing the injured part in warm but not scalding water. Sometimes cooling water for boat engines has been used for this purpose. There is no evidence that hot water denatures the venom: indeed, the pain often returns instantly when the heat treatment is stopped. Local anaesthetics may give some relief, but in a severe case a regional nerve block may be indicated, as are systemic opiates. Antivenom rapidly reduces symptoms, especially when given early.

The use of a tourniquet after a stone fish sting will do nothing but increase the patient's discomfort and enhance the local necrotising effects of the venom. In Australia arterial tourniquets are not recommended in the management of any type of envenomation. In most cases, such as those of snake bites, the pressure immobilisation technique is used,⁵ which has been shown successfully to retard the movement of venom from the bitten or

stung region. In the case of stone fish poisoning, however, it is best that the concentrated necrotising venom is allowed to diffuse freely away from the region. Deaths due to the systemic effects of the venom are extremely rare, with only a couple recorded in published work.

Infection often occurs with this type of injury. It should be remembered that marine bacteria comprise a wide range of organisms, and many are resistant to common antibiotics and also may require saline media for culture. It follows that debridement should be assisted by washing the wound well with fresh or preferably sterile water. The drug of first choice is trimethoprim-sulphamethazole. Tetanus prophylaxis should also receive attention.

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- 1 Wilmhurst P. Stone fish bite. *Br Med J* 1990;300:436. (17 February.)
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Analysis of serial measurements in medical research

SIR,—Dr J N S Matthews and colleagues have made a spirited case for the use of the summary measures approach to the analysis of repeated measures.¹ Though this is undoubtedly one of the best methods, their claims for it are extravagant.

Two of their objections to an analysis at each time point also apply to summary measures. If univariate analyses are performed on maximum values and on areas under the curves for subjects in a clinical trial the facts that these measurements come from the same subjects and are not independent are also ignored. Many of the summary measures that are commonly used together are correlated even when the measurements on which they are based are not. The summary measures approach is more reasonably recommended on the grounds that it may be a sensible way to reduce data; it is not more valid than an analysis at each time point, the validity of which was noted by Yates in the paper cited by Dr Matthews and colleagues.²

The authors are also uncritical in their recommendation of the measures used in clinical pharmacology. Many of these are not good measures, and their common use is as much a matter of illogical habit as is the analysis at each time point performed in other subjects. The widespread use of the poor "time to event" measures betrays an ignorance of the way in which causality is determined in experiments. For example, in a single dose placebo controlled trial of a bronchodilator a "return to baseline" of forced expiratory volume in one second (FEV₁) in the bronchodilator group may be observed some hours before the mean FEV₁ in the bronchodilator group equals the mean in the placebo group simply because the whole experiment is affected by a strong downward trend (the patients may have been imperfectly "washed out," they may become tired with the FEV₁ manoeuvre, etc). Under such circumstances a comparison between groups at each time point to determine the duration of action of the bronchodilator, although not without difficulties, is better than defining duration in terms of the conceptually false "time to return to baseline."

Despite these criticisms it is pleasing to see space given to an article on this topic. If the authors'

general advice on thinking carefully about measurements and ways of combining them when planning experiments is followed current practice will improve considerably.

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- 1 Matthews JNS, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. *Br Med J* 1990;300:230-5. (27 January.)
- 2 Yates F. Regression models for repeated measurements. *Biometrics* 1982;38:850-3.

AUTHORS' REPLY,—We are grateful to Dr Stephen Senn for his comments and for this opportunity to emphasise and clarify some of the points in our paper.

We agree with Dr Senn that the principal advantage of summary measures is that they are chosen to address specific questions and to have a meaningful interpretation. The success of the method rests entirely on the appropriate choice of the summary measures. This should depend on a careful consideration of the aims of the study and perhaps an inspection of the data rather than on any of the illogical habits mentioned by Dr Senn.

The dependence between successive values of the original variable is likely to be high, and this will make it impossible to correctly interpret, for example, levels of significance calculated at successive time points. Two summary measures may well be dependent, but this position is different in at least three ways: firstly, each summary is intended to answer a separate question, and dependence with other measures does not invalidate the analysis; secondly, choosing summary measures of different aspects of the response may lead to measures that are not as highly correlated as the original variables; and, thirdly, the nature of the dependence between summary measures may be of interest in itself (something unlikely to be true of the original values) and can be investigated by standard statistical methods.

The analysis of serial measurements is not straightforward, and inevitably we had to exclude many topics from consideration in our paper. Among these was the difficult topic of interpreting and analysing data when interest may legitimately be focused on whether and when a patient has returned to a pretreatment level or to an equilibrium state. The time to an event may be a very valuable summary measure, but if the event is difficult to define sensibly or precisely then its value may be wholly undermined. At this stage we would simply remark that inspection of the shapes of the responses would be important. Once again we must emphasise that appropriate summary measures can be sensibly chosen only on the basis of a thorough understanding of the measured variable and the purpose of the study.

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Superglue inadvertently used as eyedrops

SIR,—The problems associated with dropper bottles of similar appearance were emphasised by Mr Christopher Lyons and colleagues in their report of nail adhesives being administered instead of eye drops.¹

As previous attempts at limiting the appearance of non-medical plastic bottles have not been taken up the authors suggest that a distinctive shape should be adopted for ophthalmic dropper bottles. This confusion with glue and nail fixer bottles is not, however, the only danger of multiple dose ophthalmic dropper bottles. They also allow cross infection and the risk of irritation from the preservatives used in multiple dose formulations.

Perhaps it would be better to overcome all such dangers and abolish multiple dose containers for ophthalmic use and change to sterile, plastic, single dose units for all therapeutic eye drops and ointments. Labelling can be inscribed on the flange attached to the single dose unit in Braille as well as clear text, and each unit can be taken off, used, and discarded for each dose application.

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- 1 Lyons C, Stevens J, Bloom J. Superglue inadvertently used as eyedrops. *Br Med J* 1990;300:328. (3 February.)

Training in accident and emergency

SIR,—We would like to add our comments to those of Mr Francis Morris and colleagues.¹ We have run an induction course at our hospital on the first two weekends of February and August since 1985, enabling accident and emergency departments to send half of their new senior house officers on one weekend and half on the other.

An analysis of 1431 assessment forms returned during 1985 to 1989 (20 courses) showed that 1412 participants found the course useful. Of 22 topics, the most useful were head injuries; gynaecological emergencies; limb injuries; major injuries; minor injuries; spinal problems; radiological pitfalls; and eye, ear, nose, and throat, and dental emergencies. This probably reflects the delegates' lack of experience with these types of problems. As a result of feedback we have added psychiatric emergencies and common orthopaedic mistakes to the course programme.

Our attempts to test skills objectively have included a comparison of the performance of the senior house officers at the hospital during the first week of August 1987. Among the tutored doctors one incorrect and 46 correct assessments of radiographs were made compared with 16 incorrect and 98 correct assessments made by untutored doctors (0.02 < p < 0.05).

Many consultants in accident and emergency medicine support the course, and we think that all senior house officers in this subject would benefit from such a period of intensive training.

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- 1 Morris F, Cope A, Hawes S. Training in accident and emergency: views of senior house officers. *Br Med J* 1990;300:165-6. (20 January.)

SIR,—We were most surprised that Mr Francis Morris and colleagues did not mention orthopaedic surgery in their study of senior house officer training in accident and emergency.¹ At least a quarter of patients seen by general practitioners' and over a third seen in the accident and emergency