

human intracisternal retrovirus. This particle (reported in *The Lancet*⁵) was found in cells from patients with multiple sclerosis, a neuroimmunological disorder.

I also object to the assessment that our work on HIAP has not advanced yet from that of a laboratory curiosity. While not establishing HIAP as the aetiological agent, our observations that more than 95% of persons with systemic autoimmune diseases such as Sjögren's syndrome and systemic lupus erythematosus have serum antibodies to the proteins of this virus established a strong linkage to these important diseases.³

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Failure of low-dose dapsone-pyrimethamine in primary prophylaxis of *Pneumocystis carinii* pneumonia

SIR,—Hughes et al¹ proposed weekly dapsone for prophylaxis of *Pneumocystis carinii* pneumonia (PCP).¹ In other controlled trials, dapsone plus pyrimethamine weekly² or twice weekly³ was effective in PCP primary prophylaxis of HIV patients with CD4 counts below 200/ μ l compared with intermittent co-trimoxazole and aerosolised pentamidine.

In an open trial we selected 197 HIV-infected patients with CD4 counts below 200/ μ l, no previous PCP, and no known allergy to study drugs. The patients were randomised to receive aerosolised pentamidine 300 mg monthly with a Respigard II nebuliser, or co-trimoxazole (160/800 mg) every other day, or dapsone 100 mg weekly plus pyrimethamine 25 mg twice weekly. Three primary end-points (death, PCP occurrence, and dose-limiting toxicity) were compared by Kaplan-Meier estimates in an intention-to-treat analysis. Supplementary analysis included censoring of patients with less than 30 days' follow-up or ineligibility for breaking the inclusion criteria or crossing over for serious adverse events (eligibility analysis). We evaluated the homogeneity of the three groups at baseline, and each variable was controlled as a predictor by Cox regression. All the procedures accorded with the ethical standards of the institutional committee on human experimentation. At enrolment 68 patients received pentamidine, 66 co-trimoxazole, and 63 dapsone-pyrimethamine. The three groups were similar in age, sex, route of HIV transmission, and CD4 count. The dapsone-pyrimethamine group more frequently had a previous AIDS diagnosis ($p=0.04$) and a lower frequency of zidovudine administration ($p=0.01$) compared with the co-trimoxazole group.

Interim analyses were planned every 5 months; the first two showed no differences between treatments. At the third, patients had been followed up for a median of 7.7 months. For PCP events, the difference between co-trimoxazole and dapsone-pyrimethamine was significant in the intention-to-treat ($p=0.0008$) and in the eligibility analysis ($p=0.001$). Cox regression controlled for all considered baseline variables and confirmed this difference in the intention-to-treat (relative risk 25.7, 95% CI 2.4-257.2, $p=0.007$) and in the eligibility approach (21.4, 1.8-247.1, $p=0.01$). The difference between dapsone-pyrimethamine and pentamidine was significant only in the eligible patients ($p=0.048$) and was confirmed by Cox analysis (6.3, 1.2-33.4, $p=0.03$). Differences between pentamidine and co-trimoxazole were not significant. Moreover, in intention-to-treat univariate analysis we observed a higher probability of 1 year survival for co-trimoxazole (85%) than for pentamidine (58%, $p=0.004$) or for dapsone-pyrimethamine

PCP OCCURRENCE AND ESTIMATED INCIDENCE DURING PRIMARY PROPHYLAXIS

Analysis	Aerosolised pentamidine	Co-trimoxazole	Dapsone-pyrimethamine
<i>Intention-to-treat</i>			
No of cases	68	66	63
PCP episodes	4	1	9
Probability of PCP at 1 yr	0.11	0.03	0.33
<i>Eligibility</i>			
No of cases	50	54	48
PCP episodes	3	1	8
Probability of PCP at 1 yr	0.12	0.03	0.33

(47%, $p=0.002$), but the Cox model showed a negative independent effect of treatment on survival for dapsone-pyrimethamine only compared with co-trimoxazole (2.8, 1.1-7.3, $p=0.037$). We observed 85 adverse reactions in 14 342 patient-days (events per 100 patient days = 0.59) with pentamidine, 110 reactions in 18 124 patient-days (0.6) with co-trimoxazole, and 101 reactions in 10 372 patient-days (0.97) with dapsone-pyrimethamine. However, only 3 pentamidine, 7 co-trimoxazole, and 7 dapsone-pyrimethamine patients discontinued treatment because of a serious adverse event (not significant).

These results showed a significantly lower efficacy for low-dose dapsone-pyrimethamine compared with co-trimoxazole and aerosolised pentamidine in PCP primary prophylaxis. A negative effect on survival of dapsone-pyrimethamine-treated patients compared with co-trimoxazole also occurred. The higher frequency of PCP in our study than that observed by Hughes et al¹ may be explained by the lower CD4 count in our patients (median 97/ μ l) and expression of more advanced HIV disease. Mallolas et al² also observed a higher rate of PCP occurrence with dapsone-pyrimethamine than with co-trimoxazole and pentamidine, but the differences were not significant. On the other hand Girard et al⁴ reported that daily dapsone plus weekly pyrimethamine was equally effective compared with aerosolised pentamidine, but with an additional significant protective effect against cerebral toxoplasmosis. We believe that low-dose dapsone-pyrimethamine is not a satisfactory regimen for PCP primary prophylaxis, especially in patients with advanced HIV disease. A different schedule, which includes daily dapsone with weekly pyrimethamine, should be evaluated in a large controlled trial in comparison with co-trimoxazole, considering in addition the potential effect on cerebral toxoplasmosis prophylaxis.

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Wet vacuum-cleaning and housedust-mite allergen

SIR,—Because exposure to housedust-mite allergen is important,^{1,2} we investigated intensive cleaning to reduce allergen concentrations.

Over 8 months, carpets in 20 houses in Oxfordshire were vacuum-cleaned in a standard way with the same machine (Vax 3 in 1). In 10 randomly chosen houses, we used the wet mode and a special cleaning solution (Allerite, Vax). Houses were cleaned four

WET VERSUS DRY VACUUM-CLEANING

Vacuuming	% reduction (Der p1/m ²)		% reduction (Der p1/g recovered dust)	
	Day 42	Day 182	Day 42	Day 182
Wet	62.5*	66.0†	39.8*	36.7‡
Dry	38.3	23.4	5.7	0

Paired t-test, baseline vs day 42 or 182, *p < 0.02, †p < 0.01, ‡p < 0.05

times in the first 8 weeks and three times in the next 6 months. Dust from the total area of 2 carpets in each house was collected in separate bags, sieved, weighed, and extracted.¹ Der p1 was measured in an ELISA.³

Both wet and dry vacuum-cleaning reduced total recoverable dust by 69% on day 42 and 61% on day 182, both times being 4 weeks after the last cleaning. The failure of dry vacuuming to reduce allergen concentrations (ie, Der p1 per g fine dust) presumably reflected the equal removal of both allergen bearing and non-allergen bearing dust particles (table). However, the total allergen recoverable was decreased, but the reduction failed to reach statistical significance.

The wet procedure reduced the mean recoverable allergen per square metre vacuumed by two-thirds (table). But there was less reduction in mite allergen per g of recovered dust, by about one-third. When all time points were considered, the maximum reduction of Der p1 per m² vacuumed by the wet procedure increased to 76% (p < 0.005, best time vs baseline), compared with 54% when measured as Der p1 per g of dust.

The ability of the wet procedure to reduce recoverable allergen and hence patients' exposure by 75% indicates that high-surfactant solutions can dislodge mite faecal particles (95% of accumulated allergen is in this form). The rapid fall in concentrations supports cleaning as the predominant mechanism of action, although enhanced mite removal must lead to decreased allergen production over the longer term. Residual solvent could also have a direct effect on the mite, although the solution is dilute and most is recovered.

Allergen concentration in dust (Der p1) is the measurement used in clinical studies. We believe that exposure cannot be assessed as µg/g because total recoverable dust is ignored. Certainly cleaning cannot be studied in this way. Overall exposure can be assessed only as total recoverable dust (ie, g/m²). This measurement is most likely to correlate with airborne allergen concentrations, probably the best index of natural exposure⁴ but one that has practical difficulties.

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Magnetic resonance imaging in epilepsy

SIR,—Your Aug 8 editorial discusses the assessment of hippocampal sclerosis (HS) by magnetic resonance imaging (MRI), and concentrates on techniques for quantification of hippocampal volume. In addition to volume assymetry, three other MRI features of HS have been reported: loss or disruption of internal structure, decrease in signal on T1 weighted images, and increase in signal on T2 weighted images.¹ Quantification improves the estimation of hippocampal assymetry which is often visible to the naked eye on

appropriately orientated MR images. The quantification of T2 relaxation times, available on most commercial MRI systems, similarly enhances identification of HS.²

Although a single MR feature of HS can be used to diagnose most cases of HS, undue reliance on any one can be misleading. Hippocampal atrophy (although possibly not assymetry) is a feature of several neurological diseases, including Huntington's disease, amnesic states,³ and Alzheimer's disease,⁴ and HS can exist without measurable hippocampus assymetry.⁵ Similary, T2 signal can be increased in the hippocampus in situations other than HS—for example, foreign tissue lesions, and hamartomas—and care should be taken to minimise partial volume effects. It is the concordance of features of HS, either assessed qualitatively or quantitatively, which helps to achieve the best MRI-based diagnosis and enables its detection in difficult cases.

Hippocampal size varies greatly between healthy individuals. In consequence, bilateral abnormalities, which are present in a high proportion of histologically verified hippocampal sclerosis,⁶ may never be detectable by measurement of hippocampal volumes alone. By contrast, the range of normal hippocampal T2 relaxation times is small. This potentially enables identification of subtle and bilateral hippocampal abnormalities.⁷

Although conceding the close relation between increased T2 signal and HS, you state "gliosis per se does not result in prolonged T2 relaxation". The relation between gliosis and T2 signal is more controversial than this statement would imply. In rats treated with vigabatrin, T2 relaxation times were prolonged by an average of 7 ms (about 10%) in vivo in areas of cortical gliosis, where no other histopathological change was present.⁸ Barnes and co-workers' data⁹ also show a trend towards prolonged T2 relaxation times within the areas of gliosis in their experimental model of cortical injury. We suggest that gliosis may itself prolong T2 relaxation, and that this is a probable explanation for raised T2 signal in features associated with gliosis such as HS, brain scars, and gliotic hamartomas.

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Improvement in seizures after ivermectin

SIR,—After the first round of ivermectin mass treatment for onchocerciasis in Kabarole district, Uganda, some epileptics from two communities reported improvements in seizure patterns. To follow up these reports, all epileptics in these communities were asked to come for examination, and 91 met criteria for inclusion in this survey (48 men). The mean age was 15.9 years (range 6-50) and, on average, 4.1 months had elapsed between ivermectin treatment and examination (2.5-13.0). Grand mal seizures were present in 69 and petit mal in 22.