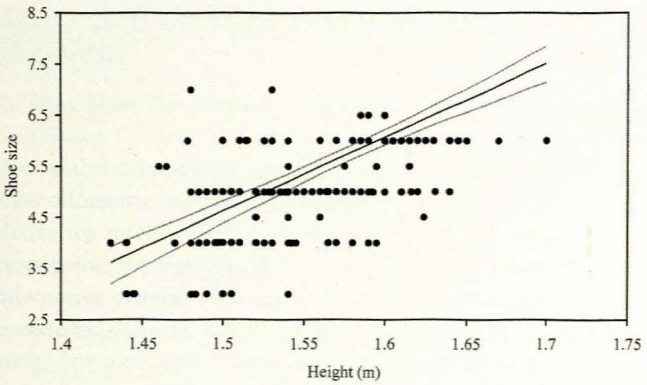

Fig. 1. Scatter plot of maternal shoe size against maternal height. The solid line represents the relationship predicted by the regression: y = 14.0 (SEE 1.1) · x –16.3 (SEE 1.8); F = 151.42, df = 1 and 213, P < 0.001; adjusted r^2 = 0.41. The dotted lines represent the 95% confidence intervals of the regression line.

(r^2 = 0.41) as that observed in Van Bogaert's study (r^2 = 0.12).[1] Nevertheless, there was only a modest tendency towards an increased risk of caesarean delivery for mothers with smaller shoe sizes and those with shorter statures (model 1, Table I) — even selecting those cut-offs for shoe size (below size 7) and stature (below 1.60 m) that displayed the strongest bivariate associations with caesarean delivery (analyses not shown). The statistical strength of these associations did increase after controlling for maternal and neonatal factors that were significantly associated with an increased risk of caesarean delivery (BMI, previous caesarean delivery and macrosomia; models 2 and 3, Table I), but none achieved statistical significance (models 2, 3 and 4, Table I). Instead, caesarean deliveries were up to three times more common among mothers who were obese (> 29 kg/m^2) before delivery, while mothers who had already had at least one previous caesarean delivery were more than twice as likely to have another.

These findings suggest that neither shoe size nor stature were important (or useful) risk factors for caesarean delivery in this population. Either they had a limited predictive value for pelvic (in)adequacy, or they were perceived as irrelevant by those deciding whether to perform a caesarean delivery. Given that only half of the obstetric records examined in the present study contained records of maternal shoe size, and fewer of these also contained maternal height measurements, it is likely that the clinicians responsible for collecting this information share the view of the World Health Organistation (WHO) collaborative panel, which recently concluded that stature did not meet the screening criteria for assisted delivery.[6]

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PLANT STEROL/STEROLIN SUPPLEMENT USE IN A COHORT OF SOUTH AFRICAN HIV-INFECTED PATIENTS — EFFECTS ON IMMUNOLOGICAL AND VIROLOGICAL SURROGATE MARKERS

To the Editor: It has been demonstrated that micronutrient supplementation may be an important prophylactic and therapeutic measure for HIV-1-infected patients, and is possibly one of the few potential interventions for low-income countries.[1] In sub-Saharan countries facing the bulk of new infections worldwide, the use of highly active antiretroviral therapy (HAART) is out of reach of most patients because of the cost in the private sector and the lack of provision of any therapies by the health departments of these countries. In recent years many groups have investigated the outcomes of this infection in patients supplemented with vitamin B_2 or multivitamin supplementation including/excluding vitamin A during pregnancy.[3] Some studies have shown that high doses of vitamin B_6 supplements were associated with improved survival of patients, while zinc supplementation was associated with poorer survival.[4]

A supplement containing a mixture of plant sterols and sterolins has been developed and investigated by our group in the treatment of many diseases. This mixture has been shown to have immune modulating activities — the addition of this mixture to T-cells *in vitro* leads to the enhanced secretion of interleukin 2 (IL2) and gamma interferon (INF-γ)[5,6] and further tests revealed that the mixture preferentially targets CD4 cells of T_{H1} phenotype and leaves T_{H2} CD4 cells unaffected.[7] This mixture was tested in a double-blind, placebo-controlled manner as an adjuvant in patients with pulmonary tuberculosis and it was shown to have a positive effect on disease recovery in such patients.[8] The mixture was also tested in a double-blind, placebo-controlled trial in healthy marathon runners where it prevented exercise-induced inflammation and post-event transient immune suppression.[9] Furthermore, the beneficial effects of this mixture in an animal model of

retroviral disease (feline immunodeficiency virus (FIV)-infected laboratory cats) has been reported previously (J Lamprecht *et al.* — poster 11236, World AIDS Conference, 28 June - 3 July 1998).

Our group has been investigating the immunological benefit derived from the use of this natural mixture in a 6-year open-labelled study of HIV-infected patients. The patients were encouraged to participate in other clinical trials if they were eligible for inclusion or to use appropriate antiviral treatment if they could afford it. However, the results of the present report include only the data derived from patients not on any other forms of HIV therapy. To date, we have follow-up data from 123 patients over a period of 39 months. The patients were stratified according to their baseline CD4 cell numbers on entry and three groups were thus formed: patients with CD4 < 200/µl at baseline (N = 10), those with CD4 200 - 500/µl (N = 66), and patients with baseline CD4 > 500/µl (N = 47). All patients were followed up at monthly intervals for the first 3 months and thereafter at 4-monthly intervals. Body mass was measured at each visit and any concomitant conditions (including opportunistic infections) were noted and treated appropriately. Prophylaxis against opportunistic infections was prescribed according to accepted guidelines. Patients were questioned at every visit as to their use of any other supplements or medication — data on patients using any anti-retroviral therapy were excluded from the present analysis. The CD4 cell numbers were determined using flow cytometry on whole blood. Plasma viral loads were assayed in stored samples using automated nucleic acid sequence-based assay (NASBA). Results were expressed as number of copies per millilitre of plasma.

An independent statistician conducted the statistical analysis and used the Statistical Analysis System (SAS) mixed procedure analysis, testing for statistical differences between baseline parameters and all follow-up values for each group. Significance was set at $P < 0.05$.

We have sequential data for 21 months for the group with low CD4 numbers at baseline (CD4 < 200/µl, N = 10). They showed a statistically significant decline in the median (± standard error of mean (SEM)) percentage and absolute numbers of CD4 cells: 11 ± 1.6% and 134 ± 18 CD4/µl at baseline to 7 ± 2.0% and 23 ± 21 CD4/µl at 21 months (P = 0.01 and P = 0.001 respectively). During the same period of time, although these patients lost the immune cells, they showed no significant increase or decline in the plasma viral load as determined by NASBA: 4.23 ± 1.21 log at baseline and 4.60 at 21-month follow-up.

Follow-up data for the group with CD4 cells at baseline 200 - 500/µl (N = 66) are available for 39 months. Statistical analysis of the data shows no significant change in the median CD4 percentage (19 ± 0.7% versus 18.5 ± 1.7 %; not significant (NS)), median CD4 absolute count (median 349 ± 11 versus 275 ± 19 CD4/µl blood, NS) as well as the plasma viral load (5.06 ± 0.81 log versus 5.15 ± 0.84 log, NS).

The patients who were the most immunologically intact (CD4 > 500/µl at baseline entry) showed significant changes only in the virological parameters measured over a period of 39 months. These patients (N = 47) exhibited no significant change in the CD4 cell percentage (median 29 ± 0.9% versus 28.5 ± 4.7%, NS), no significant change in the median CD4 cell absolute counts (646 ± 30 versus 639 ± 67 CD4/µl blood, NS) but a significant decrease in the plasma viral load (4.59 ± 0.45 log versus 3.11 ± 0.38 log, P = 0.038; Fig. 1). The interesting observation within this group is the fact that 7 patients within this group (7/47, 15%) had reached undetectable plasma viral load (NASBA, detection limit of 200 copies/ml of plasma) within 12 months of starting the study. No correlation was found between the ability of such individuals to reach undetectable viral loads within 12 months and either their baseline viral loads or their baseline CD4 count. We can only assume that this feature is linked to an innate immunological feature that remains unclear at present. Such features may include cytotoxic T cell (CTL) activity as described in long-term non-progressors and non-infected sexual contacts of infected patients,[10,11] or the ability to mount and maintain a beneficial cytokine response.[12] We have recently shown that patients who have used the sterol/sterolin mixture for at least 12 months exhibit a predominant T_{H1} cytokine response *in vitro* suggesting that the mixture could possibly maintain a beneficial CD4 cell response leading to effective CTL activity.[7] However, we have not determined sequential CTL activity in the patients using the mixture.

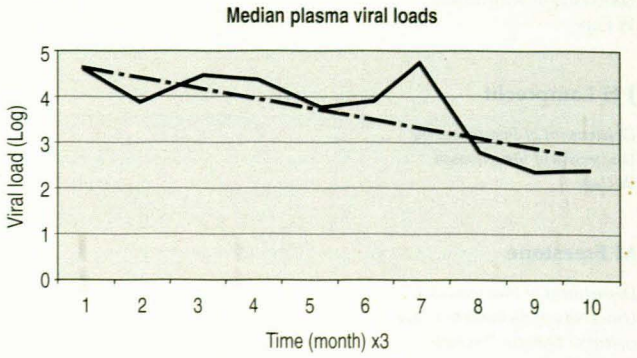

Fig. 1. Median plasma viral loads in the patients in group 3 (CD4 > 500/µl at entry) showed a significant 1.48 log drop in viral load over 30 months. The dashed line indicates the trend of the actual values (solid line) at each time point.

The results of this pilot study open up new avenues that need to be explored. Since the plant sterol/sterolin mixture was tested in an open-labelled manner in this group of infected patients, new clinical trials must be initiated under strict placebo-controlled trial conditions to prove efficacy. Such studies are currently planned. However, considering the

manner in which it impacts on the cells of the immune system, it is not surprising that only the group of individuals who begin the study with high CD4 cell counts would benefit if the surrogate markers CD4 and viral loads are analysed and used as endpoints of such a study. This mixture has no anti-retroviral activity as determined by *in vitro* p24 production by infected human lymphocytes (data not shown). Therefore, it stands to reason that new studies must be directed at patients who are newly diagnosed shortly after infection. However, the group of individuals whose infection is long-standing may still derive benefit in the absence of any therapy, as is the scenario in Africa. In such patients perhaps the most relevant primary endpoints (surrogate markers) of efficacy would include mortality, rate/incidence of infections requiring intervention, hospitalisation, etc. We have already shown that such patients, despite the loss of CD4 cell numbers over the study period, maintain their body weight, a marker that would indirectly indicate disease progression.

This study also introduces the possibility of investigating the use of this natural immune-modulating mixture together with a simple and less expensive regimen of enhanced monotherapy (such as didanosine and hydroxyurea) or pulse therapy using combination therapy when required to control viral replication. This scenario is possibly the most appropriate for Africa where the costs of such drugs are prohibitive to the majority of infected patients.

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USE OF ALTERNATIVE MEDICINE BY PATIENTS WITH NEUROLOGICAL DISEASE

To the Editor: After publication of a paper on alternative medicine (AM) in this *Journal* in 1999,[1] several further cases of inappropriate management by AM practitioners were seen at Wentworth Hospital. This observation prompted a study to determine the extent and type of AM used by an inpatient population.

Patient use of AM was determined by means of a questionnaire. Questions included the type of AM use, mode o therapy, cost, and explanation given by the AM practitioner. The findings were compared with final conventional medicine (CM) diagnosis and treatability of the condition.

There were three groups of patients: those who had sought the help of AM practitioners (N = 32), those who did not (N = 41) and cases where information was not available (N = 7).

In the AM group all but 1 patient attended a traditional healer; the majority of these patients were given oral medication. Eleven of these 31 patients (35%) did not know the cost of treatment as a relative had paid the fees. Two patients were treated for free. The fees charged for the remaining 18 respondents ranged from R20 - R2 000, to a goat, to an ox plus a goat. While this study did not address the financial status of the patients, virtually all those from a disadvantaged background are classified as 'H1' individuals by the hospital. Such patients are charged an all-inclusive fee of R134 per month of hospital stay. The majority of these patients did not pay hospital fees at all. The diagnoses given to the patients by the AM practitioners and the corresponding CM diagnoses are listed in Table I.

Sixty-three per cent of the AM patients said that they were not given an explanation of the findings. This observation is