dicative of a global immune system recovery following antiviral therapy.

AVIDAN U. NEUMANN[1,2] &
GUY GOROCHOV[1]
[1]*Laboratoire d'Immunologie Cellulaire CERVI URA CNRS 625, Hopital Pitie-Salpetriere 83 Boulevard de l'Hopital 75013 Paris, France.*
[2]*Department of Life Sciences, Bar-Ilan University, Ramat-Gan 52900, Israel.*

Connors and Lane reply — Without seeing the data cited by Gorochov *et al.* it is impossible to comment on the validity of conclusions drawn from their own data. With regard to the data presented in our paper, we can respond to the three points raised:

The three patients in our study received potent anti-retroviral therapy including indinavir sufficient to give dramatic increases in $CD4^+$ T cell counts. Two of these patients received only two infusions of IL-2 which is unlikely to result in the observed increases in $CD4^+$ T cell counts. Further, data within the paper show that IL-2 causes a preferential increase in naive $CD4^+$ T cells which one would expect to be a more polyclonal population[3] and therefore more likely to show less skewing of size patterns after therapy, rather than more, as suggested. If restoration is to be observed one would choose patients with low CD4 counts prior to therapy and substantial increases after therapy. The patients in the study were carefully selected from a large cohort for just those criteria.

Secondly, Gorochov *et al.* are correct in pointing out the effects of $CD8^+$ T cell contamination. However, only one sample had 90% purity and of the other samples in question, only the pre-therapy sample on patient 11 had 95% purity. All others were >98% pure. Also, preliminary experiments were carried out to determine the number of cells necessary to provide consistent results in advanced patients without sampling error. Changes in the repertoire observed subsequent to therapy on less than 10 million highly purified $CD4^+$ T cells are not interpretable.

Finally, comparing the four peaks surrounding a major peak allows analysis of all major disruptions. Smaller peaks at each end of the distribution are low in intensity and more variable and therefore not included in the analysis. In fact, inclusion of those peaks yields misleading results.

It is important that restoration of the repertoire is not confused with improvements observed in functional or phenotypic analyses or in the clinical status of the patient. Indeed functional improvements following anti-retroviral therapy may be mediated *in vitro* or *in vivo* by proliferation of existing low frequency clones and may occur in the absence of restoration of all of the clones which may mediate resistance to opportunistic infections in an HIV uninfected individual.

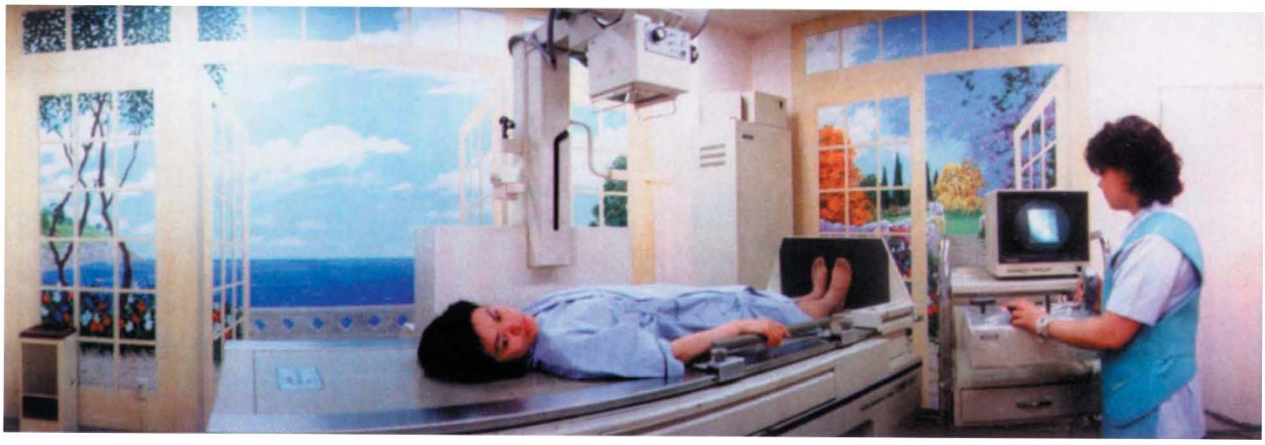
In the context of immune reconstitution and $CD4^+$ T cell repertoire restoration, it is important when interpreting data that one considers how advanced is the disease prior to therapy and the level of their response to therapy. Undoubtedly one will observe some change in some of these parameters in some patients. However in the three patients we studied intensively, this was not observed. Our data and recently published clinical data[4] indicate that immediate reconstitution of the repertoire and restoration of clinical resistance to opportunistic infections is not the rule.

MARK CONNORS & H. CLIFFORD LANE
Laboratory of Immunoregulation
National Institute of Allergy and Infectious Diseases, National Institutes of Health
Building 10, Room 11B-13
10 Center Drive
Bethesda, Maryland 20892-1662

1. Connors, M. *et al.* HIV-1 infection induces changes in CD4+ T-cell phenotype and depletions within the CD4+ T-cell repertoire that are not immediately restored by antiviral or immune based therapies. *Nature Med.* **3**, 533–540 (1997).
2. Autran, B. *et al.* Positive effects of combined anti-retroviral therapy on CD4+ T cell homeostasis and function in advanced HIV disease. *Science* (in the press).
3. Schwab, R. *et al.* Expanded CD4+ and CD8+ T cell clones in elderly humans. *J. Immunol.* **158**, 4493–4499 (1997).
4. Jacobson, M.A. *et al.* Cytomegalovirus retinitis after initiation of highly active antiretroviral therapy. *Lancet* **349**, 1443–1445 (1997).

Correction
In the above mentioned article by Connors *et al.* the abstract referred to therapy with IL-12. This should have read IL-2.

... a thousand words



Asahi Shimbun

Images that soothe — Japanese hospitals help patients relax by giving their normally drab walls a lick of paint. Here the Fijieda Heisei Kinen Hospital in Shizoka Prefecture, west of Tokyo, surrounds patients with ocean and garden. —R.N.