whether the hypotheses have survived critical review by fellow scientists, and, as *Frye* suggested, the acceptance of the knowledge or technique in the pertinent field. *Frye* was not the wrong standard. It was just too simplistic. Science is not simple, and we fool ourselves looking for magic bullets to help courts deal with it without doing the work. Yes, *Daubert* is complex. Hopefully, it is complex enough to handle the complexities of expert evidence.

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1. See, generally, D. L. Faigman, D. H. Kaye, M. J. Saks, J. Sanders, *Modern Scientific Evidence: The Law and Science of Expert Testimony* (West Group, St. Paul, MN, ed. 2, 2002).

Supplementing Antiretroviral Therapy

JON COHEN'S ARTICLE "CONFRONTING THE limits of success" (News Focus, 28 June, p. 2320), which discusses the limits of antiretroviral therapy (ARV) in managing HIV disease, overlooks an important area of research. People with access to ARV have been using a variety of interventions, notably, dietary supplements as defined by the Food and Drug Administration, to prevent or manage the immediate and delayed side effects of ARV.

Unfortunately, the majority of HIV-infected individuals do not have any access to ARV. The World Health Organization has estimated that nearly 80% of the world's population relies on botanical and other indigenous medicines as their primary source of healthcare (*1*). Some of these traditional medicines may be helpful in slowing the progression of HIV and are beginning to be investigated.

There is modest research on the use of supplements to counteract drug side effects or modulate immunity and on the use of traditional medicine against HIV, but the scope of this research is limited. One study showed the benefit of glutamine in offsetting diarrhea resulting from protease inhibitor treatment (*2*). Acetylcarnitine is being assessed at the Royal Free Hospital in London for its effect in managing neuropathy related to nucleoside analog therapy.

However, a great deal more clinical data are needed to evaluate the benefits, risks, and limitations of such interventions. Certain botanicals, multivitamins, and B-complexes have shown some efficacy in slowing HIV progression (*3*–*7*). Could some combination of low-cost and locally available interventions help to delay progression and provide hope as ARV is slowly being introduced to resource-poor areas?

The long-term impact of ARV interventions may not be fully understood, but we certainly understand the outcome of failing to treat people with HIV. Methodologically rigorous and ethically sound clinical studies of botanical and dietary supplement interventions must be undertaken immediately and vigorously.

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Alternative HIV Vaccine Strategies

IN HIS EDITORIAL "STEERING A COURSE TO AN AIDS vaccine" (28 June, p. 2297), David Baltimore succinctly expresses the despair concerning the development of an effective vaccine against HIV infection. He notes the difficulties in raising antibodies and cytotoxic lymphocytes (CTL) to a virus that mutates rapidly. Indeed, escape from CTL is the hallmark of simian immunodeficiency virus (SIV) infection and CTL with high avidity can rapidly select for escape variants (*1*). In the same issue, Jon Cohen ("Monkey puzzles," News Focus, 28 June, p. 2325) describes the pessimism regarding basing an effective vaccine on CTL mechanism (*1*, *2*).

However, there is an alternative strategy to the prevalent approach of using HIV proteins or DNA. We have been guided by "experiments of nature," preventing HIV infection by targeting either alloimmunity (*3*, *4*) or the CCR5 coreceptor of HIV (*5*).

HIV virions contain HLA class I and II proteins (*6*), and alloimmunity may play a role in HIV transmission from infected mothers to

their offspring (*7*), in protection of female sex workers (*8*), and in inhibition of HIV in adults (*9*, *10*). The most consistent protection against SIV infection in macaques has been immunization with inactivated SIV grown in human CD4$^+$ T cell lines in which the HLA antigens elicit effective immunity to SIV (*4*).

About 1% of the Caucasian population has a homozygous 32–base pair deletion of CCR5; these individuals do not express cell-surface CCR5 and, with very few exceptions, are completely resistant to HIV infection (*11*). An HIV-CCR5 vaccine strategy may have a dual effect of targeting not only the virus but also its major receptor. Indeed, we have developed a macaque model based on targeting not only SIV envelope and core antigens but also CCR5, using the 70-kD heat shock protein (HSP70) as an adjuvant that generates the CC chemokines (CCL3, 4, and 5) and interleukin-12 (*5*, *12*). Preliminary results suggest that clearance or decrease in the viral load can be elicited by this immunization strategy and challenge with SHIV 89.6P (*13*).

Both of these alternative strategies of immunization are independent of HIV mutation and CTL escape. The mechanism of protection does not focus on either CTL or neutralizing antibodies, but on integrating the immune repertoire of innate and adaptive immunity.

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Envelope-Based HIV Vaccines

HIV RESEARCHERS EVERYWHERE ARE GRATEful to *Science* for featuring HIV in their 28 June issue to coincide with this year's AIDS Congress in Barcelona. However, there are two points in Jon Cohen's article "Monkey puzzles" (News Focus, p. 2325) that require further consideration.

First, the statement that "monkey studies with AIDS vaccines have completely failed to elicit antibodies that can neutralize the virus" (p. 2325) is not consistent with the published data. Many papers have shown the ability of envelope-based HIV vaccines to induce antibodies that neutralize T cell line–adapted virus isolates, although neutralization of primary CCR5-dependent HIV-1 isolates was rarely observed. In contrast, our papers clearly show that immunization of Rhesus macaques with a plasmid DNA vaccine prime followed by a recombinant oligomeric V2 loop–deleted SF162 envelope protein boost is capable of inducing serum antibodies that neutralize multiple primary isolates of HIV-1 that are both antigenically distinct and CCR5-dependent (*1*, *2*). To our knowledge, this was the first time that a vaccine-induced immune response was shown to be capable of broad primary isolate neutralization, and we are dismayed that this significant milestone in HIV vaccine research is overlooked by a review in a widely read journal.

Second, the table on p. 2326 ("AIDS Vaccine Pipeline") does not include vaccines in preclinical testing sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) in collaboration with Wyeth Laboratories and Chiron Corporation (a version of the DNA prime-protein boost vaccine mentioned above). These IND-enabling preclinical studies are supported by the NIH HIV Vaccine Design and Development Team Contracts, which have been well publicized. We believe that underreporting the breadth and scope of NIAID's commitment to research and development of HIV vaccines does this important agency a great disservice.

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Response

THE PIPELINE TABLE SHOULD HAVE MADE clear that the list was not all-inclusive. The Chiron and Wyeth studies appear on a more comprehensive pipeline table that accompanied an article that I wrote for the 2 March 2001 issue ("AIDS vaccines show promise after years of frustration," News Focus, p. 1686). That article includes a prediction from Chiron that its vaccine would be in human trials in 2002 (which does not look likely now), and it describes the work in some detail. The assertion that antibodies have "completely failed" to neutralize the virus in monkey studies may be a bit of an overstatement, but not much, as is clear simply by look-