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Seeing cause for optimism. *Dani Bolognesi points to several promising developments in AIDS vaccine work.*

all of them has been limited by their side effects. But newer work is showing that lower doses may not only minimize the drugs' harmful side effects, but may actually increase their benefits.

"We tended to [approach the] drugs with an oncology point of view, that it's probably better to give a little more," says Thomas Merigan of Stanford University. "Now we're in a more chronic disease treatment mode. With less [drug], we may be able to get more enduring effects on T4 cells; that's really going to be exciting, and we may hear more about that at the meeting."

If low doses can reduce the side effects of ddI and ddC, making them clinically useful drugs, says Merigan, they will likely be useful in alternation with AZT to prevent HIV from developing drug resistance.

There are several potential AIDS drugs that act at sites other than reverse transcriptase, although it is too soon to tell how effective most of them will be since they have had little or no clinical testing yet. For example, the protease inhibitors, which block an enzyme needed for the formation and maturation of AIDS virus particles, are just beginning to move from test tube to clinical studies, says Robert Yarchoan of the National Cancer Institute, but clinicians will be eager to hear the reports on them at San Francisco because the drugs may provide a second point of attack on the AIDS virus.

Meanwhile, α-interferon is one drug that already has shown promise in clinical trials. In a recent development, Clifford Lane of the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland, and his co-workers published a study in the 1 June issue of the *Annals of Internal Medicine* that indicated that the interferon slows the development of disease in people who are infected by the AIDS virus but not yet symptomatic. Even if drugs such as interferon don't turn out to be as effective as AZT, Lane says they offer promise in combination therapy. The early results of such combination regimes should be presented at the conference.

The molecular biology of the AIDS virus will also be a major topic at the conference and a recent finding in that area may shed some light on one of the enduring mysteries of the AIDS epidemic: Where did the virus come from? The epidemic only became apparent about 10 years ago. Had the causative agent been present in isolated groups and not noticed until it made its way into the more general population? Or was it new to the human population, perhaps transmitted from another primate?

In the 24 May issue of *Nature*, Simon Wain-Hobson and his colleagues at the Pasteur Institute report that they have isolated a virus from the chimpanzee that may be the missing link in HIV-1 evolution. The new virus is more closely related to the AIDS virus than any of the other animal and human immunodeficiency viruses found so far.

If the virus is a bona fide chimpanzee virus, Desrosiers wrote in an editorial accompanying the article, that might suggest that chimpanzees were the source of human HIV-1. But even if they were, Wain-Hobson points out, that doesn't mean that transmission to humans was coincident with the beginning of the AIDS epidemic. It could have occurred 100 or more years ago, and only blossomed into an epidemic with recent population movements.

But wherever the AIDS virus came from it has now spread around the world. And while the activists will be sounding a loud message that governments should be doing more to combat the disease, the quieter message coming from the scientists is that the AIDS virus is yielding its secrets, but slowly. ■ **MARCIA BARINAGA**

One Step Closer for Gene Therapy

Later this year, a young child whose life is threatened by severe immune deficiency disease is likely to be the first patient to receive true human gene therapy.

Last week the National Institutes of Health's human gene therapy subcommittee unanimously endorsed a proposal by R. Michael Blaese of the National Cancer Institute to try to correct ADA, or adenosine deaminase, deficiency by inserting the ADA gene into patients who are not doing well with alternative methods of treating this disease. The disease leaves its victims vulnerable to infections that usually take their lives during adolescence, if not before.

For some of the world's handful of ADA patients (there are probably no more than 50 worldwide) bone marrow transplantation has proved to be a useful therapy. Others are resisting infection with the help of a drug called PEG-ADA, which is injected once or twice a week. But some patients are not good candidates for marrow transplantation and are not doing well enough on PEG-ADA to be considered effectively treated. (The drug is not a cure.) It is these patients—perhaps four or five in number—who will be considered for the NIH experiment.

The subcommittee's enthusiastic endorsement of the experiment, a collaborative study that also includes W. French Anderson and Kenneth Culver of the heart institute, and NCI surgeon Steven A. Rosenberg, came as something of a surprise in light of the panel's fractious review of a draft of the protocol 2 months ago (*Science*, 13 April, p. 159). By contrast, last week's meeting was a paradigm of reasoned discourse.

In the interim, two things happened to change the subcommittee's collective mind. First, Blaese and Anderson redrafted their protocol, making substantive changes that included a new definition of which patients will be eligible for the first trials. In addition, colleagues in Italy completed studies in SCID mice (animals with severe combined immunodeficiency) that provide good experimental data to support the likelihood that the Blaese-Anderson experiment will work.

Technically, the subcommittee's approval at its 1 June meeting was provisional, pending further modifications in the gene therapy protocol that were worked out during the meeting. If all goes well, final approval will come on 30 July when the subcommittee meets jointly with its parent body, the NIH's recombinant DNA committee whose "Yes" vote is also required before final approval is sought from the director of NIH and the Food and Drug Administration which also has jurisdiction.

■ **BARBARA J. CULLITON**