People with HIV get immune-reviving drug

A naturally produced protein can renew human immune systems damaged by the AIDS virus, researchers reported this week. This marks the first time anyone has demonstrated significant, long-term boosts in infection-fighting white cells.

H. Clifford Lane of the National Institute of Allergy and Infectious Diseases in Bethesda, Md., and his colleagues knew that interleukin-2 can spur the growth of certain immune cells. They wondered whether a regular regimen of this protein would shore up an immune system besieged by HIV, the virus that causes AIDS.

To find out, they gave 25 HIV-infected people infusions of interleukin-2 for 5 days every 2 months over a period of at least 8 months. The group reports its findings in the March 2 NEW ENGLAND JOURNAL OF MEDICINE.

The researchers first studied 10 recruits with moderate immune suppression; they had CD4 T lymphocyte "counts" of greater than 200 per cubic millimeter of blood. Physicians often use a decline in T lymphocytes to indicate a progressing disease.

T cell counts for 6 of the 10 people rose more than 50 percent after a year. Counts for the remaining four volunteers either worsened or remained stable during the same period.

Some of the patients who improved showed a dramatic response to the therapy. For example, one recruit's T cell count rose from 554 to a robust 1,998. People with a healthy immune system usually have a T cell count ranging from 800 to 1,200.

"It's unprecedented," says Lane, who has worked on interleukin-2 therapy for 13 years. With conventional anti-HIV drugs, "you don't see counts go up like this," he adds.

The team also showed that 7 of the 10 people had at least a 25 percent decline in the cells that carry a molecule associated with disease progression. This finding suggests that the drug has slowed the infection, at least in some cases.

Next, Lane and his colleagues turned to 15 volunteers with severely impaired immune function; all had T cell counts of less than 200. Only two of these recruits showed a 50 percent increase in T cells after therapy. The remaining 13 didn't get much benefit from the treatment, the scientists report.

The drug doesn't appear to work well in people with an immune system gutted by HIV. "I think there's too much virus around," Lane says, adding that once HIV has the upper hand, it may be difficult for the immune system to recover, even with the help of interleukin-2. Chiron Corp. of Emeryville, Calif., produced the interleukin-2 used in the study.

For HIV-infected people at an earlier stage of T cell loss, interleukin-2 treatment may provide a respite from the onslaught of HIV. The hope is that periodic infusions of interleukin-2 will maintain critical levels of T cells and thus ward off the opportunistic infections that plague AIDS patients.

Yet interleukin-2 remains a relatively toxic drug. It provokes a severe, flulike illness, and its side effects include rash, nausea, diarrhea, and depression.

What's more, the researchers remain uncertain about its safety for HIV-infected people. Specifically, they worry that interleukin-2 treatment could lead to an increase in viral replication.

Using a sensitive test, Lane and his team found a short-term upswing in the amount of HIV RNA in the blood of 4 of the 10 patients with T cell counts over 200. This despite the fact that all the patients took a standard antiviral drug such as AZT while participating in the study, Lane points out. So far, that burst of virus has been transient.

This research offers no proof that interleukin-2 provides HIV-infected people with fewer infections or a longer life. Future research must show "whether or not there's a clinical benefit associated with this increase in CD4 count," Lane says. — *K. Fackelmann*

Origins of life: Keys to an early chemical

Given the intricacy of life's molecular processes, questions surrounding the earliest biochemistry loom large. How, for instance, did life's key chemical components arise on Earth — and in what order?

Addressing these questions, Anthony D. Keefe, Gerald L. Newton, and Stanley L. Miller, all chemists at the University of California, San Diego, describe in the Feb. 23 NATURE, a possible pathway for the evolution of an important biological molecule. They report synthesizing, in conditions similar to those most likely present on early Earth, the molecule pantetheine.

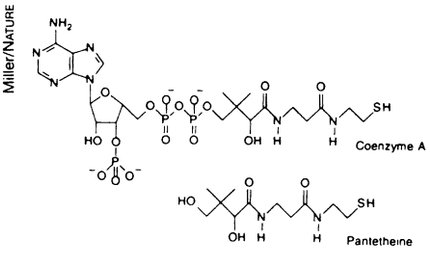
Pantetheine forms a chunk of a larger molecule, coenzyme A. Because coenzyme A acts in conjunction with other enzymes to facilitate reactions in living organisms, the authors believe it may have "acted in this capacity very early in the development of life on Earth."

Among other things, coenzyme A helps amino acids hook together and aids in making peptides. Both functions may have supported early evolution of proteins and nucleic acids, such as RNA and DNA.

Moreover, the building blocks of coenzyme A "have been shown to be probable prebiotic compounds," the chemists observe. In their current experiment, they show that pantetheine can form at temperatures as low as 40° Celsius, in circumstances typical of evaporating bodies of water beside beaches and lagoons. "These results suggest that pantetheine could have been a component of the prebiotic soup," they say.

While stressing that "nobody knows the exact sequence of events that led to life," Miller adds that "this finding opens many questions." For instance, if coenzymes appeared before life, "they may have helped make certain chemical pathways more efficient. It's possible that coenzymes became involved in important reactions even before there were living organisms."

Miller/NATURE



Pantetheine fits into coenzyme A.

Had the building blocks of coenzyme A emerged independently near lakes or oceans, they could have been incorporated more easily into early self-replicating chemical systems or metabolic cycles, he adds.

"Coenzyme A looks like a prebiotic type of molecule because it seems to have formed from assorted building blocks, such as nucleotides and amino acids," says James P. Ferris, a chemist at Rensselaer Polytechnic Institute in Troy, N.Y. "You get the feeling the molecule formed in a mixing pot of prebiotic precursors."

Pointing out the versatility of coenzymes, Ferris adds that "they may have survived because they can do some tasks that neither nucleic acids nor proteins can do."

"This work is significant because it supports the idea that these component molecules may have been around on the early Earth, reacted together, and survived because they were useful to proteins and nucleic acids."

Indeed, Miller highlights the point that the reactions leading to pantetheine could occur at a mere 40°C, close to the temperature of a rocky surface on a July day. Miller now wants to search for other molecules that might have formed at the edge of a warm beach. — *R. Lipkin*