Depression, early death noted in HIV cases

Depressed men in the early stages of infection with the AIDS virus (HIV) suffer a more rapid physical decline than their nondepressed counterparts and die sooner, according to a report presented last week at the VIII International Conference on AIDS in Amsterdam. The six-year study indicates that HIV-infected men suffering from moderate to severe depression lose greater numbers of an important disease-fighting cell, tend to develop AIDS more quickly, and die sooner than their nondepressed counterparts.

"We don't know the causal connection [among these factors]," asserts physician Jeffrey H. Burack of San Francisco General Hospital, who directed the investigation. "But treating depression might potentially slow the progression of HIV disease."

Burack's findings challenge the conclusions of two previous studies in which depression and stress exerted no measurable effects on immune function among HIV-infected men (SN: 4/6/91, p.216).

Both prior investigations lasted for only six months, too short a period to pick up important immune and health effects of depression, Burack contends.

His group analyzed data collected between January 1985 and January 1991 from 330 gay and bisexual men taking part in a larger investigation known as the San Francisco Men's Health Study. Upon entering the project, all participants tested positive for HIV, but showed no signs of AIDS.

The researchers assessed depression with a 20-item questionnaire used in many epidemiological studies of mental disorders. Although the questionnaire falls short of a clinical diagnosis, 65 men — nearly 20 percent of the sample — indicated they had symptoms associated with moderate to severe depression, Burack says.

CD4 cells — important components of the immune system often used to chart the progression of HIV infection — declined significantly more each year during the study among depressed men than among nondepressed males. The plummet from a normal CD4 count to a depleted count, at which point serious infections can occur, took an average of more than five years among nondepressed HIV-infected men, but only three years, eight months among their depressed counterparts, Burack says.

Over the course of the study, about one-third of both depressed and nondepressed participants died. But during the first three years of the project, 17 percent of the depressed men died — twice the mortality rate of the nondepressed group. The two groups also displayed comparable AIDS rates at six years. However, at three years, 22 percent of depressed volunteers had been diagnosed with AIDS, compared with 15 percent of nondepressed controls.

Depression waxes and wanes over time, which may explain the erasure of differences in death rates and AIDS diagnoses between three and six years after the study began, Burack notes. His team is now analyzing depression scores obtained from participants two, four, and six years after completing the initial questionnaire. This will provide a more sophisticated breakdown of the HIV-related health risks associated with depression, Burack contends.

In the meantime, accelerated CD4 declines and death rates in the three years following HIV infection appear linked to depression, he says. Some unknown viral process may promote both depression and immunological deterioration following HIV infection, Burack theorizes. Alternatively, depression may hasten disease progression, either through direct effects on the immune system or in indirect ways. For instance, depressed men may show less willingness to seek out medical treatment and a greater tendency to engage in unhealthful behaviors.

"Treating depression can certainly improve the quality of life of men with HIV infection," Burack remarks. "Our study suggests that it may be able to prolong their lives as well." *— B. Bower*

Disarming, combating a tropical parasite

The parasites responsible for the devastating skin ulcers of the tropical disease leishmaniasis use one of the body's own chemicals to evade destruction by the immune system, according to a new study. A second report suggests that extremely low doses of a *Leishmania* parasite might serve as a vaccine to prime the body's defenses against this marauder.

The World Health Organization estimates that *Leishmania* microorganisms currently infect 12 million people worldwide, from the jungles of India and the Amazon basin to the deserts of northern Africa. Spread by several species of blood-sucking sand flies, these protozoans cause disfiguring open sores at the sites of infection. In some cases, the parasites migrate to internal organs such as the liver and spleen. This causes a potentially fatal, wasting disease named kala-azar — Hindi for "black sickness," so called because of the victims' darkening skin.

Ironically, *Leishmania* wreaks its devastation by infecting macrophages, white blood cells that normally gobble up and digest bacteria and other microorganisms. In one new study, a group led by Steven G. Reed of the Seattle Biomedical Research Institute found that the parasites survive the hostile environment inside macrophages by prompting the cells to produce large amounts of transforming growth factor-beta (TGF-beta). Macrophages normally make this chemical after they have eradicated an infection, in order to neutralize the bleach-like compound they use to kill microbes.

Reed and his colleagues report in the July 24 SCIENCE that injections of TGF-beta rendered normally resistant strains of mice susceptible to ulcers caused by *Leishmania*. Moreover, they found that injections of antibodies that block TGF-beta helped the mice fend off preexisting *Leishmania* infections.

"We think that TGF-beta production is a very early event in *Leishmania* infection," concludes Reed. "Basically, the parasite has figured out a way to keep the macrophages from killing it."

Reed says his group is now evaluating several chemical compounds that either block TGF-beta or prevent its production. He hopes to use these compounds in a cream to eliminate the skin ulcers of leishmaniasis. Currently, the only treatment for leishmaniasis is a salt made from the toxic metal antimony, which has dangerous side effects and must be taken intravenously every day for several weeks.

David L. Sacks, a leishmaniasis researcher at the National Institute of Allergy and Infectious Diseases in Bethesda, Md., says the study by Reed's group represents the first time researchers have successfully combated an ongoing leishmaniasis infection with a drug other than antimony. "This is extraordinary," says Sacks. "It has important implications for developing better treatments for this disease."

In a separate study, a group led by Peter A. Bretscher at the University of Saskatchewan in Saskatoon evaluated a potential vaccine against leishmaniasis. Bretscher and his colleagues found that they could protect susceptible mice from subsequent *Leishmania* infection by inoculating them with 330 to 1,000 live parasites.

In the July 24 SCIENCE, Bretscher's group reports that such low doses of parasites raised the number of white blood cells in the mice without actually causing disease. Sacks, however, remains skeptical. "I don't understand how this could work," he says, because sand flies often transmit leishmaniasis by transferring fewer parasites than the number in the Canadian team's vaccine.
— C. Ezzell