Relocation of Gut Bacteria Linked to Low CD4s

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In some people living with HIV, bacteria normally contained within intestinal lymph nodes are relocated to the blood stream. This process is associated with a lack of increase in CD4 cells—even in people whose HIV viral load is undetectable—according to a study in the October 1 issue of *AIDS*.

An increasing number of studies over the past several years have indicated that the decline of the immune system in HIV disease can be linked, at least in part, to the early destruction of lymph nodes in the intestines. Scientists believe that hyper-inflammation of the immune system by HIV leads to scarring of the lymph nodes, which in turn allows bacteria that are normally contained in the gut to relocate to the circulating blood in the body.

Giulia Marchetti, MD, PhD, of the University of Milan in Italy, and her colleagues thought that lymph node damage in the gut and the consequent relocation of gut bacteria might help explain why some people do not have significant increases in CD4 cell counts after starting antiretroviral (ARV) therapy, despite achieving and maintaining undetectable viral loads. Such individuals are usually called immunologic non-responders (INRs): Their HIV is suppressed by ARVs (virologic response), but their CD4 cell counts don't rise (immunologic non-response).

Dr. Marchetti's team enrolled 24 INRs and 11 full responders (FRs—who achieve both suppressed virus and an increase in CD4 cells through ARV treatment). The researchers compared both groups with 12 people living with HIV who had advanced HIV disease, but who had not yet started ARV therapy. All three groups were evenly matched in terms of age; in both the INR and FR groups, those on ARV had been taking the drugs, on average, for just over one year. The average CD4 count at the time of the study was 158 for the INRs, 824 for the FRs and 114 for those not on treatment.

The team found that the untreated patients had the strongest sign of immune activation, as measured by levels of circulating lipopolysaccharide (LPS) proteins. INRs also had elevated LPS levels compared with the FRs. The team then conducted DNA analysis of blood to detect bacteria that are usually confined to the gut. They performed this test on blood samples of seven members of each of the three groups and found that all seven of the untreated patients and five of the INRs had detectable bacteria in blood. None of the seven FRs, however, had detectable bacteria.

The authors stress that while relocated gut bacteria was associated with a lack of CD4 increase despite virologic control, the study does not prove that the relocated bacteria caused the lack of CD4 increase. Nevertheless, they recommend further research, which would seek to confirm their findings and explore interventions to control relocated gut bacteria and reduce immune inflammation.

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