IMMUNE RESTORATION: Overview

WHAT IS IMMUNE RESTORATION?

Immune restoration means repairing the damage done to the immune system by HIV.

In a healthy immune system, there is a full range of CD4 cells (T-cells) that can fight different diseases. As HIV disease progresses, the number of CD4 cells drops. The first CD4 cells that HIV attacks are the ones that specifically fight HIV. Some types of CD4 cells can disappear, leaving gaps in the immune defenses. Immune restoration looks for ways to fill these gaps.

A healthy immune system can fight off opportunistic infections (OIs). Because these infections develop when CD4 cell levels are low, many researchers think that CD4 cell counts are a good measure of immune function. They believe that increases in CD4 cell counts are a sign of immune restoration. There is some disagreement on this point. See "Are New CD4 Cells As Good As Old?" below.

HOW CAN THE IMMUNE SYSTEM BE RESTORED?

If antiretroviral therapy (ART) is started immediately after someone is infected with HIV, the immune system won't be damaged. Unfortunately, very few cases of HIV are identified that early. See fact sheet 103 on acute HIV infection. As HIV infection continues, it can damage the immune system. Scientists are exploring several ways to repair this damage.

Improving the function of the thymus:

The thymus is a small organ located at the base of the throat. It takes white blood cells that come from the bone marrow and turns them into CD4 cells. It works the hardest when you're just 6 months to two years old. It starts to shrink when you're in puberty. Scientists used to think that the thymus stopped working by the age of 20. However, research shows that it keeps producing new CD4 cells much longer, maybe until age 50. Strong ART can allow the thymus to replace lost types of CD4 cells.

When scientists thought that the thymus stopped working at a young age, they studied transplanting a human or animal thymus into someone with HIV. They also tried to stimulate the thymus using thymic hormones. These methods might still be important for older people with HIV.

Restoring the number of immune cells:

As HIV disease progresses, the numbers of both CD4 (T4) and CD8 (T8) cells drop. Some researchers are trying to maintain or to increase the numbers of these cells.

One approach is called **cell expansion.** An individual's cells are multiplied outside the body, and then infused back into the body. A second approach is **cell transfer**. This involves giving a patient some immune cells from the patient's twin or an HIV-negative relative.

A third method uses **cytokines**. These are chemical messengers that support the immune response. The most work has been done on interleukin-2 (IL-2), which can lead to large increases in CD4 cells. Fact Sheet 482 has more information on IL-2.

Another approach is **gene therapy**. This involves changing the bone marrow cells that will travel to the thymus and become CD4 cells. Gene therapy tries to make the bone marrow cells immune to HIV infection.

Letting the immune system repair itself:

CD4 counts have increased for many people who have taken ART. Some scientists believe that the immune system might be able to heal and repair itself if it's not fighting off large numbers of HIV viruses. This approach seems more likely now that we know that the thymus keeps working until a person is almost 50 years old.

Most people take medications to prevent opportunistic infections (See Fact Sheet 500) when their CD4 cell counts go below 200. However, if these people take antiretroviral medications and their CD4 cell counts climb back over 200, it is safe in most cases to stop taking medications to prevent these infections. **Be sure to talk to your health care provider before you stop taking any medication.**

Stimulating HIV-specific immune response:

Researchers used a modified, killed HIV virus (Remune®) to stimulate the body's response to HIV. Remune is essentially the same as a vaccine, but it is given to people who are already HIV-infected. Years of research produced confusing and disappointing results. New approaches are being studied. One of these is a therapeutic vaccine called DermaVir. It is applied to the skin. DermaVir is being tested in a Phase I/II study.

A combination of HIV vaccines and interleukin-2 (IL-2) increased anti-HIV immune responses and led to immune control of HIV for up to a year in one study. Fact Sheet 482 has more information on IL-2.

An "immune regulating hormone," Immunitin or HE2000, is being developed by Hollis-Eden Pharmaceuticals. It showed good results in a Phase II clinical trial.

ARE NEW CD4 CELLS AS GOOD AS OLD?

Most approaches to immune restoration try to increase the number of CD4cells. This is based on the assumption that when CD4 cells increase, the immune system is stronger.

When people with HIV start taking ART, their CD4 cell counts usually go up. At first, the new CD4 cells are probably copies of existing types of CD4 cells. If some "types" of CD4 cells were lost, they won't come back right away. This could leave some gaps in the body's immune defenses.

However, if HIV stays under control for a few years, the thymus might make new CD4 cells that could fill in these gaps and restore the immune system. Some of these CD4 cells might help control HIV infection.