

Human Growth Hormone for Thymus Reconstitution



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the impact of therapies on the thymus are of great interest to those researching immune restoration approaches.

Striking data were presented on the use of human growth hormone (rHGH) and its impact on thymus reconstitution in people with HIV. A study evaluating the use of rHGH for treating lipodystrophy (body composition changes) was conducted using doses ranging from 1.5 to 3.0mg/day for six to twelve months. In a sub-study, CT scans (a type of x-ray) were taken of the thymus on five volunteers before, during and after using rHGH. All had been on stable anti-HIV therapy for 1–4 years and had very low HIV levels in their blood, most below the limit of detection of the viral load tests. The mean CD4+ cell count was about 419.

Marked increases in thymus mass at six months were noted, beyond what have been seen using anti-HIV therapy alone. This increase was sustained over the course of rHGH therapy and correlated with an increase in naïve T-cells, most notably naïve CD4+ cells—suggesting that the thymus is functioning properly and contributing to new T-cells. The development of new, naïve T-cells is critical to true immune restoration. When rHGH therapy was stopped, there was a coincident deterioration in thymus mass. CD4+ cell count increases observed over the course of therapy, however, were sustained despite this deterioration.

While these data are encouraging, they do not yet lead investigators to the conclusion that broad and general use of rHGH be recommended for immune restoration therapy. Two of the five volunteers discontinued rHGH therapy due to side effects. Of note, rHGH can cause arthralgia (joint pain) and glucose intolerance, increasing risks for diabetes. Further, investigators caution against the use of over-the-counter or through-the-internet purchase of products claiming to contain human growth hormone. Some of these products claim to contain plant-derived growth hormone, others claim to contain cow (bovine) or goat-derived growth hormone and still others claim to contain substances that increase the body's production of HGH. There is no evidence that any of these products contain either a relevant product or a dose needed to induce the types of effects seen in the study. Over-the-counter and internet-based sales of claimed growth hormone products are a major source of health fraud. Moreover, Dr. Napolitano cautioned that this was a small study and it is too early to draw conclusions about the role of rHGH in immune reconstitution. A larger study has been designed and is enrolling volunteers.

The thymus is an important immune organ necessary for development of new T-cells (like CD4+ and CD8+ cells.) Without some residual thymus, immune reconstitution with a wide variety of functional CD4+ cells is not believed to be possible. Thus, the state of the thymus in HIV disease and

Another study evaluated immune responses in 12 people with lipodystrophy who received, in conjunction with anti-HIV therapy, 12 weeks of 4mg/day growth hormone and then received either placebo, every other day, rHGH or twice weekly rHGH for an additional 12 weeks. Volunteers were then followed and monitored for 24 weeks off all rHGH therapy. HIV-specific CD4+ and CD8+ cell responses were evaluated before, during and after rHGH therapy.

After 12 weeks of rHGH therapy, marked improvements in HIV-specific CD4+ and CD8+ cell responses were observed in 9 of 12 volunteers. These improved responses did not correlate with improvements in overall CD4+ or CD8+ cell counts or decreases in HIV levels. Improved HIV-specific CD4+ cell responses were lost by week 24, regardless of whether an individual continued on any rHGH regimen or received placebo. Improved HIV-specific CD8+ cell responses were sustained in all groups (including the placebo group) for this second 12-week period. By the end of the 48-week study period, HIV-specific CD8+ cell responses were waning and HIV-specific CD4+ cell responses remained undetectable.

Herpes-specific CD4+ cell responses were present at study entry and improved over the 12 weeks of rHGH therapy. During the maintenance phase of the study, the subsequent 12 weeks of lower rHGH doses or placebo, these responses fell to below pre-study levels. The loss of herpes-specific CD4+ cell responses correlated with symptoms of herpes.

Investigators conclude that 4mg/daily rHGH therapy may be able to improve both HIV-specific CD4+ and CD8+ cell function. The effect on CD4+ cell function does not appear to be sustained with reduced doses or when rHGH is stopped.

Herpes-specific immune responses are also improved over the 12-week rHGH therapy period and lost thereafter. While rHGH may bolster cellular immune responses in the short-term, during higher dose daily therapy, it might also be correlated with a longer-term loss of these functions—as herpes-specific responses were actually higher prior to initiating rHGH than after the end of the first 24 and 48 weeks of study. This provides reason for caution around the use of rHGH for immune reconstitution outside of studies. While there is certainly interesting and compelling information coming out about the use of rHGH, enthusiasm should be tempered as further work is needed to define the true risks and benefits.

