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# EDITORIAL

# Treatment of Anorexia and Weight Loss with Concentrated Megestrol Acetate in Patients Infected with the Human Immunodeficiency Virus

The stimulation of appetite and maintenance of body weight are highly regulated physiological processes. Appetite is controlled by a large number of mediators, including hormones derived from the gut (eg, somatostatin and cholecystokinin), adipose tissue (eg, leptin, adiponectin), and brain (neuropeptides such as alpha-melanocyte stimulating hormone, corticotropin-releasing hormone), among others. Unintended weight loss and cachexia can be a pathophysiologic manifestation of a broad variety of diseases encompassing infection, malignancy, endocrine dysfunction, gastrointestinal disorders, and systemic inflammatory diseases. The loss of appetite with weight loss warrants clinical evaluation given the high likelihood that it is a manifestation of cancer, depression, or chronic infection. Patients with human immunodeficiency virus (HIV) infection often present with anorexia and cachexia. Weight loss in these patients is associated with more rapid progression of disease, lower quality of life, and increased susceptibility to the development of other comorbidities which can further lessen life expectancy.

Megestrol acetate is orexigenic and has long been used to promote appetite and weight gain independent of fluid retention in patients with cancer and other wasting diseases, such as HIV infection. Megace is a steroidal progestational agent. Chronic use of this drug can be associated with some increased risk for developing diabetes mellitus, Cushing's syndrome, and suppression of the pituitary-adrenal axis. Megace therapy is approved by the United States Food and Drug Administration to treat the anorexia and weight loss seen in patients with HIV infection.

In this issue of the *Journal of Applied Research*, Wanke and coworkers compare the effects of a concentrated formulation of megestrol acetate (Megace ES; Par Pharmaceutical, Spring Valley, NY) to conventional Megace in patients infected with HIV and losing weight on highly active antiretroviral therapy. Patients for the most part were recruited from India and South Africa. Virtually

immediately, the Megace ES therapy was associated with more rapid weight gain compared to Megace and the effect was sustained for the full 12 week duration of the trial. Importantly, there was a trend toward greater curve separation as a function of time that was statistically significant throughout the course of the trial. Appetite was significantly improved as was quality of life. Cortisol suppression was short-lived and serum cortisol levels returned to normal within 1 month of Megace discontinuation. There was no increased risk for developing diabetes mellitus and lipoprotein parameters remained stable during the 3 months of therapy. Positive changes were noted in both treatment groups for body mass indices and triceps muscle mass, important increases in patients prone to cachexia. Both groups of patients experienced increases in their white blood cell counts in response to either preparation of Megace, but the investigators did not determine if these changes were accompanied by a rise in CD4 counts.

The authors point out that they were unable to correlate changes in weight with CD4 counts or serum viral loads. This will be important to delineate further. However, Megace ES does offer a means by which to more rapidly increase weight and body mass index. It remains to be determined if this increase in rate of weight gain is associated with reduced predisposition to secondary infection, decreased morbidity, and increased life expectancy. Given the large number of people throughout the world impacted either directly or indirectly by the epidemic of HIV infection, these are issues worth evaluating further. It would be of interest to determine if this is associated with any change in survival or resistance to secondary infection. Other extant issues include determining the safety of long-term use in patients with chronic HIV infection, further exploration of the precise mechanism(s) by which Megace is orexigenic and stimulates weight gain, and the durability of weight gain once Megace is discontinued.