

LIPOWATCH[®]

NEWS

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The LipoWatch program from Visionary Health Concepts is designed to support providers and patients with education that integrates a "real world" focus with scientific data. The last three faxes discussed lipid-lowering agents. This month we focus on the challenges in developing a definition of lipodystrophy. NOTE: prior LipoWatch faxes are archived on the web at http://www.vhconcepts.com/edu_progs.cfm.

The 4th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV was held September 22 to 25 in San Diego, California. Over 100 basic science and clinical studies were reported. The workshop provided additional evidence that any definition of lipodystrophy will be difficult to develop. *In vitro* results often conflict with *in vivo*; short-term results with longer-term, and different drugs within a single antiviral class may have very different effects.

For example, Steven Teitelbaum from Washington University of St. Louis discussed protease inhibitors and bone mineral density. Protease inhibitors were initially suspected of decreasing bone mineral density. Teitelbaum, however, showed that while indinavir interferes *in vitro* with bone formation, ritonavir appears protective by interfering with bone resorption.

The metabolic substudy of ACTG 384 showed very different results at different time points. Limb fat actually increased

through the 16-week time point, after which it decreased faster for patients taking d4T/ddl than those taking AZT/3TC. From week 32 to week 64, limb fat was above baseline for the AZT/3TC group, but below baseline for the d4T/ddl group. By the end of the study at 80 weeks, limb fat had decreased from baseline levels in all patients (but more in the d4T/ddl group.) This highlights the need for long-term follow-up of patients on any antiviral therapy (and helps explain the often conflicting results observed from many, often disparate, short-term studies)

In a satellite session, Andrew Carr and Carl Grunfeld each presented their work on defining lipodystrophy. Carr, using a methodology from auto-immune diseases, selected lipodystrophy cases and controls from HIV+ patients. He looked for objective parameters that distinguished between the two groups. In a multi-center, multinational study, he developed a criteria for, if not a formal definition of, lipodystrophy based solely on objective parameters. The model includes gender, age, duration of HIV infection, CDC disease category, waist-to-hip ratio, HDL cholesterol, anion gap, visceral to subcutaneous adipose tissue ratio (based on CT scan) and trunk-to-limb fat ratio (based on DEXA scan). The values are adjusted and compiled to give a lipodystrophy score. The definition was presented in February 2002¹ but has not yet been published. Carr plans to have

a lipodystrophy "calculator" using his definition available on a web site.

Grunfeld presented partial results for men from his FRAM study, which did not include any assumptions about elements of lipodystrophy. Using an age-matched HIV-negative control group, he isolated factors statistically linked to HIV or to each other. Surprisingly, fat accumulation was not statistically linked with HIV-related lipodystrophy. It occurred both in men with HIV and in the controls, but was more common in the controls. Grunfeld also found more buffalo humps (fat accumulation behind the neck, or dorso-cervical fat pad) in controls than in men with HIV.

Not everyone agrees on the need for a complete definition of lipodystrophy. While many argue that it is needed to conduct careful clinical trials into the causes of the syndrome, the Adult AIDS Clinical Trials Group (AACTG) has been screening patients into studies based on selected physical measurements or laboratory indicators (e.g. waist/hip ratio or fasting insulin level) relevant to the particular study question. In terms of treatment, the need for a definition is not at all clear, as all treatments studied so far are linked to specific symptoms much more than to the overall syndrome. It is clear, however, that more work will be done in this area. ■

¹Carr A et al. An Objective Case Definition of HIV Lipodystrophy. Abstract 31. 9th Conference on Retroviruses and Opportunistic Infections, Seattle, 2002.

Next month's LipoWatch will discuss fillers/implants used in reconstructive surgery in patients with facial wasting.

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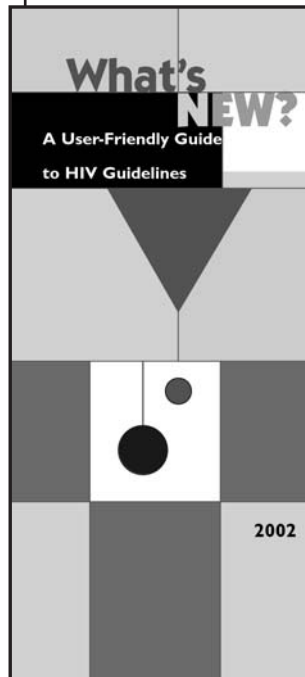
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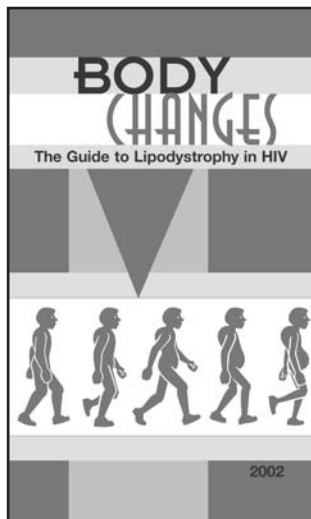
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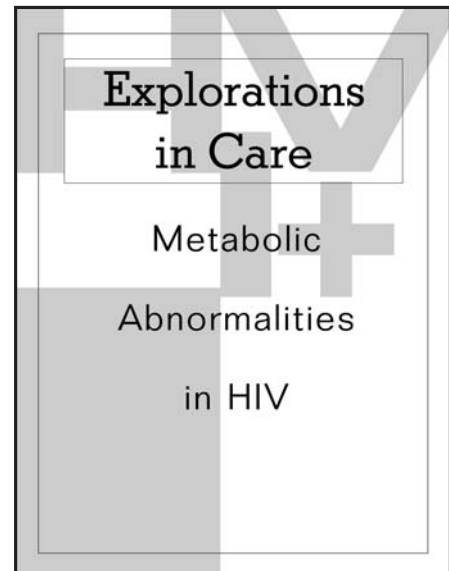
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