

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. This month's fax discusses current knowledge on antiviral regimens that are less likely to cause the symptoms associated with lipodystrophy. NOTE: LipoWatch faxes are archived on the web at http://www.vhconcepts.com/edu_progs.cfm.

There is a growing body of research on the pharmaceutical management of metabolic complications in people taking HIV anti-retroviral medications. However, because of the desirability of low pill burdens and the challenge of sometimes complicated drug interactions, most patients and physicians would prefer to avoid these complications in the first place. Initially, the research on metabolic dysfunction focused on protease inhibitors⁽¹⁾ so initial attempts to reduce lipodystrophy entailed protease-sparing regimens. Later, the NNRTI efavirenz was shown to increase cholesterol. More recent work documents that NRTIs also contribute to these problems, especially fat wasting⁽²⁾. There are no simple medication recommendations for avoiding or minimizing lipodystrophy symptoms.

Some studies document associations between individual antiviral agents and metabolic symptoms. The most frequently implicated drug is stavudine. It is not surprising that some of the earliest "switch" studies designed to improve metabolic parameters replaced stavudine with other agents. For example, the PIILR Extension study⁽³⁾ randomized 18 patients with severe lipodystrophy to either continue on a quadruple nucleoside regimen or to switch their thymidine analogue drugs (stavudine or zidovudine) for other nucleoside analogs. The study showed only modest, transient improvements in lipodystrophy but also found that 5 of the 9 patients in the "stop" group experienced loss of virologic control.

One study of protease-sparing regimens is the Spanish NEFA study⁽⁴⁾. Four hundred

and sixty patients taking a PI, with virologic suppression for at least 6 months, were randomized to replace the PI with efavirenz, nevirapine or abacavir. There were some beneficial changes in lipids in each arm. HDL levels rose significantly with both non-nukes (but fell with abacavir). Insulin sensitivity improved in all groups. The proportion of patients with high total cholesterol levels was significantly lower with abacavir than with the non-nuke arms. Lipid improvements after switching were greater in patients without lipodystrophy than in those with the syndrome, once again underscoring the necessity for both the initial selection and development of more benign regimens.

The identification of HIV antiviral regimens that minimize metabolic disturbances is at an early stage. There is a clear need for studies specifically designed to address this issue, and of longer duration, particularly in treatment-naïve patients. The listing below must be considered preliminary. Unfortunately at this juncture, as most HIV-providers are aware, there is no antiviral regimen that is clearly free, statistically or otherwise, from the association with lipodystrophy or its associated metabolic syndromes. Even if there were, clinicians would still be compelled to consider the metabolic consequences of the implicated medications when the initial regimen(s) failed. At this point, selection of regimens should be based in part on their assumed contribution to individual aspects of the lipodystrophy syndrome and tailored to the medical condition and preferences of the patient. Non-drug factors linked to lipodystrophy, such as nadir CD4 count, family history of either early atherosclerotic disease or adult on-set diabetes, should also be kept in mind as they may help identify patients at higher risk of development of metabolic disturbances. Considerations of side effects must be appropriately bal-

anced with assessments of a prospective regimen's antiviral efficacy, toxicity, and convenience.

Symptom	Better Choices	Less Attractive	Comments
Fat Wasting	Protease inhibitors; non-nucleoside analog RTIs	Thymidine analog RTIs (stavudine, zidovudine)	Possibly caused by mitochondrial toxicity caused by NRTIs
Fat Accumulation	Nucleoside and non-nucleoside analog RTIs	Protease inhibitors	FRAM study questions link to lipodystrophy
Increased LDL Cholesterol	Nevirapine, atazanavir, abacavir	Protease inhibitors*, especially ritonavir; stavudine	
Low HDL Cholesterol	Nevirapine, efavirenz		Not studied as much as LDL or total cholesterol
Increased triglycerides	Non-nucleoside RTIs, atazanavir	Protease inhibitors*, especially ritonavir; stavudine	
Insulin resistance	Nucleoside and non-nucleoside RTIs	Protease inhibitors	May lead to frank diabetes, fat accumulation

*There are significant differences among PIs in their impact on lipid levels. For example, the MaxCmin1 study found significantly higher triglycerides and LDL cholesterol with ritonavir-boosted indinavir than with ritonavir-boosted saquinavir⁽⁵⁾. Similarly, NRTIs vary in their impact on serum lipids and on fat wasting, as shown in the Gilead 903 study⁽⁶⁾.

¹Carr A, Samaras K, Thorisdottir A, et al. Diagnosis, prediction, and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study. *Lancet*. 1999;353:2093-2099.

²Mallal SA, John M, Moore CB et al. Contribution of nucleoside analogue reverse transcriptase inhibitors to subcutaneous fat wasting in patients with HIV infection. *AIDS* 14(10):1309-1316.

³D Smith and others. Thymidine analogue withdrawal for lipodystrophic patients on protease-sparing therapy improves lipodystrophy but compromises antiviral control: the PIILR extension study. *AIDS* 2002; 16:2489-2491.

⁴Martinez E, Podzamczar D, Ribera E, et al. Switching protease inhibitors to nevirapine (NEV), efavirenz (EFA) or abacavir (ABA): a randomized, multicenter, open-label, simplification trial. Program and abstracts of the 9th Annual Retrovirus Conference; February 24-28, 2002; Seattle. Abstract LB15.

⁵Gerstoft J, Dragsted Ub, Cahn Pet al. Final analysis of a randomised trial to evaluate safety and efficacy of indinavir/ritonavir versus saquinavir/ritonavir in adult HIV-1 infection: The MaxCmin1 trial. Program and abstracts of the 42nd Interscience Congress on Antimicrobial Agents and Chemotherapy; September 27-30, 2002; San Diego, California. Abstract H-172.

⁶Staszewski S, Gallant JE, Pozniak AL et al. Efficacy and safety of tenofovir DF (TDF) versus stavudine (d4T) when used in combination with lamivudine and efavirenz in antiretroviral naïve patients: 96-week preliminary interim results. Program and abstracts of the 9th Annual Retrovirus Conference; February 24-28, 2002; Seattle. Abstract 564b.

Next month's LipoWatch fax will discuss the contributions of individual antiretroviral agents to various lipodystrophy symptoms. Order now upcoming FREE Visionary Health programs and fax 800-407-2505, or register at www.freehivinfo.com. Please print clearly

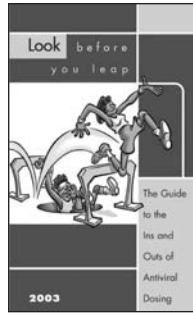
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Approx. Total # of clients		# HIV+	# HCV+	# HIV/HCV+
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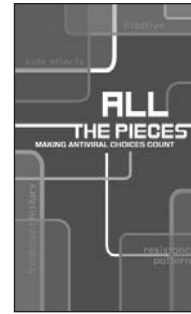


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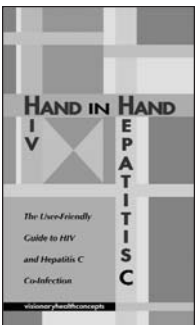
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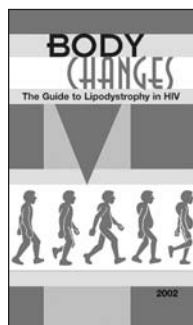


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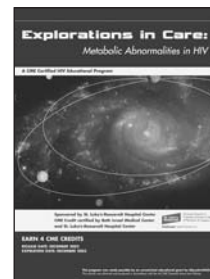


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