A New Kind of Waisting

Are drug cocktails causing ugly fat deposits?

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Justly famous for extending or even saving lives, protease inhibitors (PIs) are becoming just as famous for their drawbacks, such as cross-resistance and interactions with other medications. Now come reports that the drugs can increase levels of fat around the midriff and on the upper back, between the shoulder blades. This is not the same as the evenly distributed weight gain otherwise seen on combination therapies, and actually may coincide with the loss of lean mass in the arms and legs.

These developments have been dubbed “Crix belly”—referring to the drug Crixivan (indinavir)—and “buffalo hump.” *Crix belly* was apparently coined on an Internet chat line, but the name may be misleading. Most physicians seem to think that the problem is not with Crixivan in particular. Steven Follensbee, MD, of San Francisco suggests that people on Crixivan were simply the first to experience the paunch problem. “I can say it’s happened to at least one patient on ritonavir and to another on a saquinavir/nelfinavir combination.” In any event, he does not think the problem affects more than perhaps five percent of protease users, and, interestingly, he remembers “buffalo humps” appearing in a few patients even before PIs were available.

Jennifer Schranz, MD, of Merck Research Laboratories says that the company has received about 40 reports of fat redistribution, out of over 100,000 people who have tried Crixivan. Some of those reports included a loss of muscle in the extremities. She does acknowledge a “protease paunch” phenomenon, but believes that it is not associated exclusively with Crixivan, and perhaps not even with PIs as a class.

The “buffalo hump” was reported recently at a medical conference in Toronto. P. J. Ruane, MD, of Los Angeles, described three patients who developed uncomfortable fatty swellings at the base of the back of their necks. Each of them had CD4 counts below 200, and each had started taking Crixivan as part of their combination therapy several months before the deposits appeared. At least two of the patients were considering surgery to remove some of the fat. New York City cosmetic surgeon Jeffery Brande, MD, has successfully removed similar disfiguring deposits with liposuction, and says they did not return even when the patients continued with the same HIV therapy.

So are the fat deposits a newly discovered side effect of PIs, or are they a newly discovered symptom of HIV disease? Physicians familiar with the problem think that several dynamics may be

at work, together or separately:

Fat redistribution, like neuropathy or neutropenia (lowered white blood counts), may indeed be a long-term side effect of certain antiretrovirals. Perhaps PIs, already known to be hard on the liver, interfere with its regulation and distribution of fats.
As people on potent anti-HIV treatments live longer, they naturally experience some of the same age-related concerns facing the general population, such as middle-age bulge and high cholesterol. These may exacerbate, or be confused with, drug effects.
As viral replication is reduced, less is required of an immune system that has been working overtime for years, leaving it “disoriented” and leading to strange, unexpected responses, like fat maldistribution.

Carl Grunfeld, MD, of San Francisco says that several questions need more research. For one thing, what happens to sugar and fat metabolism in people on antiretrovirals? For another, how does the metabolism of people using HIV drugs compare with those not using them? Until these questions are answered, he offers the following advice:
Physicians should order *fasting* lab work for all patients on combination therapy; the results will yield more reliable information about fat and sugar metabolism.
Symptoms that resemble protease paunch or buffalo hump, such as Cushing’s syndrome (an abnormal fat accumulation caused by hormonal imbalance), may be serious and should be diagnosed and treated.
There may not be one monolithic new syndrome. “We may be seeing a number of different syndromes being reported at about the same time,” Grunfeld says. “Let’s do the research and get to the truth of the matter.”

In the meantime, two disturbing questions arise. First, if the hit on the liver is what’s causing this, might long-term use of these drugs cause irreparable liver damage? And regardless of the cause, could the excess fat deposits around the abdomen increase heart-disease risk, as pot guts are known to do in the overall population? Again, we don’t know. Research is urgently needed.

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