Crossing the Liver

Liver failure could get you before HIV does, and that mountain of meds you're swallowing doesn't help. Cindra Feuer tells how to make nice to this mighty organ.

September 1, 2000 By Cindra Feuer

By the fall of 1998, Beth Hastie's first HIV cocktail had caused her CD4 cells to rise and her viral load to drop to undetectable. Her cholesterol was up and the diarrhea was a drag, but, says the 30-year-old Boston AIDS activist, "my three-drug combo was doing its job and doing it well." Then her doctor tested her for signs of liver damage.

"My liver enzymes were all extremely elevated over a period of three months—a red flag," Hastie recalls. In fact, they were 10 times the normal levels, and her doctor diagnosed her with drug-induced hepatitis, meaning she had an inflamed liver. It was time to consider going off meds. "I was very conflicted. Even with the other side effects, I probably wouldn't have changed my regimen except for the liver toxicity," says Hastie, who has had HIV for 10 years. But after agonizing, she decided to go off antiretrovirals to give her liver a rest.

Subsequent research has backed up Hastie's decision. A November 1999 study showed that liver disease—whether caused by HIV meds, coinfection with hepatitis viruses, or some combination of factors—was the leading cause of death among all HIV patients at one Boston hospital, and that a third of HIVers there had to discontinue HAART to cope with liver disease. Many HIVers have preexisting conditions that make HAART even more taxing to the liver. Coinfection with hepatitis C and/or B triples the risk of liver cell death regardless of treatment regimen. Alcohol or drug use and obesity all put pressure on the liver. Women's smaller livers are at higest risk for damage.

As Hastie sees it, quelling HIV while keeping your liver happy can be a juggling act. But with a doctor monitoring liver function regularly, you can stay a step ahead of severe hepatic (liver) damage by switching drug combos, taking a strategic treatment interruption or supporting the liver with herbs and acupuncture.

The liver is the body's vital processing plant. Tucked into the lower right corner of the rib cage, it filters blood, using enzymes to metabolize toxic substances into less harmful forms. Both prescription and street drugs stress the liver. Protease inhibitors, nucleoside analogues and NNRTIs are all liver polluters, but protease inhibitors are the quickest to wreak havoc, often within a few months. Douglas Dieterich, MD, a liver specialist at Cabrini Medical Center in New York City, says that one out of five of his patients on protease inhibitors has experienced liver toxicity. He

lists the most harmful, in descending order, as ritonavir (Norvir), Crixivan (indinavir), nelfinavir (Viracept), saquinavir (Fortovase) and amprenavir (Agenerase).

A host of other drugs are also liver stressors, in particular: acetaminophen (found in many over-the-counter pain relievers), especially when mixed with alcohol; isoniazid (INH), for tuberculosis; statins, used to lower cholesterol; some cancer chemotherapy drugs; many antihypertensive agents used to control blood pressure; amiodarone and some other cardiovascular drugs; antidiabetic agents; estrogen; anabolic steroids; and some psychiatric medications.

Among HAART drugs, nukes can take longer to show their ugly side, appearing to be well tolerated for years, then causing liver damage. Certain nuke combos are particularly toxic: Some doctors mention ddI (Videx) with d4T (Zerit) as a dangerous duo. Non-nukes are easier on the liver, but may still cause damage (the European Union just issued a warning about nevirapine [Viramune]). Nukes—particularly the "d" drugs, ddI, d4T and ddC—can cause lactic acidosis, the dangerous elevation of lactic acid in the blood. Unfortunately, levels may only rise shortly before the condition becomes serious (lactate levels greater than 5 mmol/liter are dangerous). Although there was early controversy about their usefulness, it now seems that standard venous lactate levels are acceptable tests for indicating the development of this problem. Experts believe levels above 5 mmol/liter could warrant discontinuation of meds; levels below 5, but abnormal, warrant frequent monitoring.

While full-blown lactic acidosis is rare, it can be fatal. Symptoms of late stages include nausea, vomiting and shortness of breath. Anyone experiencing these may be on the way to imminent liver failure. Hastie had some palpable liver-problem warning signs—her feet and calves became swollen (edema); she felt nauseated and lost her appetite. But most people don't develop symptoms until damage sets in. Yellow skin or eyes, itching, swelling in the abdomen or legs, bruising easily, confusion, fatigue or depression may each mean, Dieterich says, that "the liver is 90 percent gone." As outward signs of liver problems are unusual, getting your enzymes checked regularly is critical for monitoring drug toxicity in the liver.

When liver cells are damaged or killed by anti-HIV drugs, liver enzymes leak into the blood. Your standard blood chemistry will include six different liver function tests, which check enzyme and blood waste product levels. Levels above normal are a warning sign of liver inflammation, or hepatitis (all liver inflammation is called hepatitis, even when it is not caused by viruses).

It is standard to check enzymes before starting a new antiretroviral regimen. For people who have a history of normal levels, Howard Grossman, MD, a clinician in New York City, recommends doing both liver function tests and a complete blood count every six weeks; for anyone coinfected with hepatitis B or C, or whose enzymes are climbing, he recommends running these tests every two to four weeks. "This aggressive approach," he says, "helps make sure we pick up the [liver] side effects before they become a problem."

When your liver is inflamed, how do you decide whether to switch, go off or stick with meds?

Though all six liver markers should be taken into account, Dieterich offers this rough guide to one important liver enzyme, alanine aminotransferase (ALT): ALT below 40 is safe; minimal elevation above 40 is unlikely to be significant; anywhere between 200 and 600 is dangerous. “Two times normal, I wouldn’t get too excited about. If they’re seven or eight times normal, I would stop everything,” Dieterich says. It is rare and controversial to stay on meds if enzyme counts rise above 600.

When Hastie’s levels shot up, she was on a combination of nelfinavir, d4T and ddI. She and her doctor set out to find the cause and eliminate it—not an easy task when all three drugs are known liver lickers. “I developed a sense that nelfinavir was the strongest drug and was taxing my system,” Hastie says. Sure enough, soon after quitting it (while remaining on the nukes) her side effects disappeared and her liver function markers improved a bit. Four weeks later, she quit her entire regimen for a month and a half. “My liver went back to normal. Once my viral load went up and my T cells went down, it was time to start meds again.” She returned to the d4T and ddI and substituted hydroxyurea (Hydrea) for nelfinavir.

For those left with few CD4s and fewer drug options, Grossman says, “The choice becomes high viral load with low T cells and getting sick that way or risking liver failure. If someone has really high numbers, you probably have to stop.”

But not necessarily for good. The liver is known for its awesome regenerative properties. A liver that is not yet seriously damaged can take as little as two or three months to restore cells to normal functioning, a respite that a break from meds may allow. “In a relatively healthy person, somebody with a T cell count of 300 or higher, you might be more prone to give their liver a rest and hope that it will rebound,” Grossman says. However, HIVers who have advanced liver disease (cirrhosis, meaning liver tissue is scarred and marked by fibrous nodules) will have greater difficulty getting back normal function; if too much of the liver tissue is cirrhotic, recovery may be impossible.

Increasingly, HIVers are complementing toxic drug regimens with natural therapies that may be liver protective. “Given the right conditions, the liver can regenerate,” says Jackie Haught, LAc. The longtime acupuncturist suggests a combo of needles and nutrients that help support liver repair for many of her HIV clients on HAART. Experts recommend nutrients that raise liver levels of glutathione, the antioxidant that’s crucial for the liver’s conversion of toxins into harmless byproducts (N-acetyl cystine, vitamins C and E, alpha-lipoic acid and glutamine); silymarin (milk thistle extract), an antioxidant and anti-inflammatory; and coenzyme Q-10, another antioxidant that supports liver cell repair. All of the above can be taken safely with antiretrovirals.

Beth Hastie
Age: 30
Tested positive: 1992
Regimen: Hydroxyurea, d4T, ddI
XTRA FX : Inflamed liver

The pains in Beth Hastie's abdomen began in the spring of 1998. "I asked my partner, who is a nurse, 'What's over here?' and pointed to my right side. She felt around and said, 'Your liver.' I made a doctor's appointment right away."

Hastie's doc used ultrasound to diagnose her with "fatty infiltration coupled with hepatic inflammation." Blood tests showed that the levels of two liver enzymes, ALT and AST, markers of liver damage, were high (see "Organ Grinders"). Her serum cholesterol and triglyceride levels had also skyrocketed. "The doctor told me these were side effects from the Viracept [in her old combo], along with the edema," lower-leg swelling that had begun a few weeks after starting the combo. "I was having pains in my legs and feet. I was also spotting between periods and had chronic diarrhea, which started after taking the combo."

A drug holiday and new regimen has restored some peace to Hastie's liver. But if she didn't live with a nurse, she says she might not have discovered the liver trouble until there was irreversible damage: "The symptoms aren't obvious. I just thought I was having trouble adjusting to the new meds. Make sure your doctor is checking your liver enzymes. Insist on it."

-Rebecca Minnich

ORGAN GRINDER

Check your liver function at least every six to eight weeks for warning signs of damage. Any value above normal may mean your liver is experiencing stress and that you should start taking steps to care for it. Values three to five times the upper end of normal signal a red alert; consult your doctor right away. Note: Each lab has its own scale, so numbers may vary slightly.

Name: AST (aspartate aminotransferase, sometimes called SGOT)
Description: a liver, heart and muscle enzyme
Normal Range: 0 to 40 IU/l

Name: ALT (alanine aminotransferase, sometimes called SPGT)
Description:a liver enzyme
Normal Range: 10 to 30 U/ml

Name: ALP (alkaline phosphatase)
Description: a liver and bone enzyme
Normal Range: 20 to 90 IU/l

Name: GGT (gamma glutamyl transferase)
Description: an enzyme present in bile and blood
Normal Range: 5 to 37 u/l

Name: bilirubin

Description: a waste product of red blood cells, processed in the liver
Normal Range: total 0.1 to 1.2 mg/dl

Name: LDH (lactic dehydrogenase)
Description: heart, liver, kidney, brain, lung and muscle enzyme
Normal Range: total 80 to 120 IU/l

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