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Twenty-five Years in the Fight Against AIDS: What Have We Learned?

Twenty-five years of fighting HIV and AIDS has taught us many hard lessons, and the learning is far from over. We've learned a great deal about the intersection of epidemics of addiction, violence, poverty and disease as well as the many ways in which politics and prejudice affect what is fundamentally a medical problem. So many have paid with their lives for the lessons learned that it is hard to remind ourselves that society is bettered by the experience. One aspect of the medical fight against HIV that should be carefully studied is what we have learned about confronting a new disease and how it might be applied in the future.

An informative contrast can be found between the 1970's "war on cancer" (generally considered a failure) and the 1980's and 1990's war on AIDS (considered one of the great success stories of modern medicine). Why did one fail and the other succeed? Though the answers are complex (and it's clear that AIDS research itself benefited greatly from the prior assault on cancer), important lessons can be drawn about why the AIDS fight has done so much, at least among those with access to care and modern medicine, to reduce the terrible suffering and death rates seen in the early years. How was this achieved? What does it tell us about fighting other illnesses?

The perceived failure of the War on Cancer left many in the scientific community humbled and the government wedded to the belief that "throwing money" at research for a disease doesn't work. Most scientists came to believe that directing research toward specific goals doesn't speed progress; that advances largely come only from serendipity and encouraging scientists to work on whatever interests them. Time and again, we were told that studying yeast cells was as likely to bring an advance against cancer as studying the cancer itself.

The AIDS experience has in many ways shown exactly the opposite. It has shown that large, consistent long-term funding—directed toward specific objectives and goals in the context of a particular disease—really can pay off. AIDS activists and supporters in Congress and the last three Administrations successfully secured major increases in funding for the National Institutes of Health (NIH). Some of the largest increases went to supporting research against HIV, allowing the NIH and in particular the National Institute of Allergy and Infectious Diseases (NIAID) to lead a full court press against the disease. Importantly, these funding levels were either increased or sustained with each passing year for nearly two decades—far longer than support was provided for the War on Cancer.

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NOTE TO THE READER: Mark Antell, an adult hemophiliac and long time member of HACA, submitted the following information for you, the reader.

Access to Investigational Drugs

For many of us who have had HepC for a very long time, the current drug therapy for HepC doesn't provide much hope. It either doesn't work for us, or is not medically appropriate. Perhaps our best hope is access to the investigational drugs that are just now becoming available. Many of us will not survive until these drugs finally attain full FDA approval.

The FDA has recently proposed some new rules to expedite patient access to investigational drugs. Their proposal can be seen at:

<http://www.fda.gov/OHRMS/DOCKETS/98fr/06n-0062-npr0001.pdf>

The public is invited to comment on these regulations through March 14. This might be a good opportunity to voice your perspective on compassionate availability of investigational drugs to patients who have no alternatives.

The 12/18 edition of New Yorker magazine has a long article on this problem called "The Right to a Trial." This article is weakly supportive of increased patient to investigational drugs. It'll likely be available at your local library.

A strong voice for greater patient access is available at: <http://abigail-alliance.org/>

Note to the Reader:

In the November 2006 issues of *HCV/HIV Today* we published the article, "Banishing Chipmunk Cheeks and Bullfrog Neck." One of our readers made the following comments:

"As a survivor of oral cancer, I know that maxillofacial radiation therapy causes soft teeth and dental caries. Most of this happens 20 years post-treatment, so patients have to balance risks and benefits—as usual. The article suggests that radiation is appropriate, as opposed to surgery, but the attendant issues are more complicated than that."

We always encourage you, the reader, to share your experiences with us.

Note to the Reader:

The numbering of the pages for the November issue was incorrect. Instead of the first two pages being "1" and "2" they were listed as "3" and "4." Therefore, the Table of Contents did not match the listed page numbers. The actual content (the articles), however, was complete. We apologize for the error and the confusion it may have caused you, the readers.

HCV/HIV Today is published bi-monthly by the Hemophilia Association of the Capital Area. Comments and questions from our readers are strongly encouraged. Please address all correspondence to Editor: HACA, 10560 Main Street, Suite 604, Fairfax, VA 22030 or call (703) 352-7641. Any information contained in this newsletter related to the diagnosis or treatment of either hemophilia, HIV or HCV is intended for educational purposes only; HACA does not recommend or discourage any specific medical services or treatments. All questions regarding medical care should be decided by patients in consultation with their physicians or medical providers. Any reader wishing to learn more about any topic contained in this newsletter can contact HACA, and will be directed to the appropriate source.

Blood Lite

Anemia Can Cause Serious Problems for HCV Patients in Treatment

By Marc S. Botts

The most significant advancement in the treatment of hepatitis C in recent years is the antiviral drug ribavirin. The combination of pegylated interferon and ribavirin has reduced relapse rates to 20 percent from 50 percent (see "Two Ribavirin Advances," *Hepatitis*, January – March 2006). But like most choices in life, the decision to treat hepatitis C virus (HCV) with interferon and ribavirin is one of risk versus reward. In addition to the possible side effects of interferon – including flu-like symptoms, fatigue, nausea, depression, anxiety, insomnia and mental confusion – patients who take ribavirin run the risk of becoming anemic.

As many as 10 percent to 15 percent of patients treated with interferon/ribavirin therapy become anemic, a condition that can be life threatening and typically requires adjustments to the medication. A complete blood count (CBC) can be used to diagnose anemia because the test includes counts of red blood cells and of hemoglobin, the iron-containing protein in red blood cells that transports oxygen. The World Health Organization defines anemia as hemoglobin levels less than 13 grams per deciliter (g/dL) in men and less than 12 g/dL in nonpregnant women.

Hemolytic anemia is a disorder in which the red blood cells are destroyed faster than the bone marrow can produce them. There are two types of hemolytic anemia: intrinsic, which is the destruction of red blood cells due to a defect within the cells themselves, and extrinsic, which occurs when red blood cells are produced healthy but are later destroyed by infection or drugs.

Dr. Mark Sulkowski, associate professor of medicine at Johns Hopkins University School of Medicine and medical director of the Viral Hepatitis Center in Baltimore, Md., says that in general, hepatitis C infection is not associated with anemia in and of itself. "However, anemia may be found in persons with advanced liver disease and those with HIV/HCV coinfection," he says. "In addition, the current standard of care for the treatment of HCV, peginterferon alfa and ribavirin, is commonly associated with significant reductions in hemoglobin and, in some patients, anemia.

"This is primarily due to the effect of ribavirin, which causes an extravascular hemolytic anemia, and to a lesser extent, due to bone marrow suppression with interferon," says Dr. Sulkowski, who notes that the differential diagnosis for anemia is very broad and may be caused by many conditions both benign and serious.

"One of the most common types of anemia in the developed world is iron deficiency anemia," he says. "However, this is quite different than what is observed in the treatment of hepatitis C, in which iron stores are typically adequate."

In most cases, he says, the anemia subsides once the treatment is stopped. "This type of anemia is reversible following the discontinuation of these medications and is not typically a long-term problem," Dr. Sulkowski says.

Hard to Handle

Sara T. Welch of Versailles, Ky., became anemic while participating in a clinical trial for HCV treatment at the University of Louisville School of Medicine. The trial was blind, meaning she was not told whether she was receiving ribavirin or a placebo. "The clinical trial I participated in began late in 2004," she says. "After being on medication for two months, my hemoglobin dropped from around 15 (g/dL) to around 10 (g/dL). I believe it rapidly dropped further to around 8 (g/dL), which is when it was decided to dose down one of the medications."

To combat the anemia, the research coordinator cut the oral dosage (ostensibly the ribavirin) by half, leaving the injected dosage (interferon) at full strength. Welch says that although the trial was blind, she is pretty sure she was given the ribavirin rather than a placebo because of the anemia she experienced. She says the anemia left her extremely fatigued and made it difficult for her to maintain her livelihood.

Don Lyons of Gaston, Ore., knows about the fatigue. A veteran of treatment for his HCV, Lyons experienced his first bout with anemia when he went on a regimen of daily injections of interferon over the course of six months in 1992. He says his doctor monitored it closely and he kept up the treatment, although the anemia took its toll on him physically.

"I could not walk up a flight of stairs without resting," he recalls. "Everything was tiring and I would have to stop and catch my breath often during any physical exertion. It would take me hours to do jobs that normally take minutes."

While Lyons acknowledges that he experienced other

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Blood Lite continued

side effects and cannot say with complete certainty that the anemia caused all of the fatigue, it was nevertheless debilitating. "I had to ask to be relieved of my management position at work until the treatment was complete. I completed the treatment (but) it failed to kill the virus," he says.

When the first combination therapy was approved using ribavirin and interferon, Lyons started another regimen of treatment. Again, the side effects were debilitating.

"That caused the worst anemia by far," he says. "I was lethargic, slept 12 to 14 hours a day and could not do physical activity without losing my breath and having to rest." While his red blood cell count never got low enough to alter the treatment, he did suspend it after 10 months because his liver function tests and viral count spiked. "At that point, my doctor and I decided it was not worth the side effects if it was not working," he says.

A biopsy showed that the damage to his liver had been abated somewhat by the treatments he endured. Determined to fight the virus, Lyons would resume treatments over the years as new drugs and protocols were introduced. In 2002, he started a short-lived regimen of pegylated interferon and ribavirin. "When Pegasys came out, my doctor and I decided to try combo treatment again. I had not ever used (pegylated interferon) so we thought it might have a different effect," he says. "I only lasted two months. My body could no longer take the side effects as well as I had when I was younger. I had had enough."

Serious Business

In some cases, anemia can be a much more serious matter that requires close supervision by doctors. "In subjects with underlying heart disease, anemia can be life threatening and induce a heart attack," says Dr. Howard J. Worman, an associate professor of medicine, anatomy and cell biology at the Columbia University College of Physicians and Surgeons in New York City. "For this reason, people with risk factors for coronary artery disease are recommended to be evaluated before receiving interferon alpha and ribavirin for hepatitis C." Because of this risk, he advises that complete blood counts be obtained at baseline and at weeks two and four of therapy, or more frequently if clinically indicated.

Dee Jones of Memphis, Tenn., says the anemia she developed two months into the combo treatment not only left her tired, but made her prone to bruising as well. "That was my first suspicion," she says. "I told the docs

and they said 'Yes, you have been anemic the whole time.'"

Jones says her doctors decided not to alter her treatment during the year-long regimen, although to battle the anemia they did suggest that she take injections of epoetin alfa (Epogen, Procrit) – a drug that has the same biological effects as endogenous erythropoietin, a glycoprotein produced in the kidneys that stimulates red blood cell production in the bone marrow.

"I refused," she says. "It would have meant another shot." Jones says she is a sustained responder to the treatment since April 2005 but that her anemia persists.

A Shot in the Arm

Like many, Alisha Ford of New Jersey battled the fatigue associated with anemia while on the combination therapy. "I felt like my life was out of control," she says. "I couldn't do basic things like folding clothes without becoming exhausted."

Rather than cut back on medication, her doctor chose to put her on Procrit, which is approved by the Food and Drug Administration for treatment of anemia in patients undergoing chemotherapy, those with chronic kidney disease, HIV/AIDS patients being treated with the antiviral drug AZT, and select surgery patients. As a specific treatment for HCV patients, however, there has not been enough study to prove its efficacy. That, however, may change.

"The standard approach to the management of HCV-treatment-associated anemia is to reduce the dose of ribavirin," says Dr. Sulkowski. "There are no adjuvant medications approved by the FDA for the treatment of anemia in this setting. However, several clinical trials support the use of recombinant human erythropoietin for the treatment of anemic HCV-infected patients receiving peginterferon plus ribavirin. Although little data is available, it is anticipated that a similar medication, darbepoetin alfa (Aranesp), will also be effective in this setting."

The effectiveness of the Procrit was a blessing for Ford, but she was battling other side effects that ultimately forced her to stop treatment. "Procrit actually helped tremendously. It gave me motivation to continue the treatment. I started to feel like myself again," she says. "The reason I stopped the treatment is because I was losing too much weight and I was severely depressed."

Despite the debilitating side effects, Ford doesn't think others should be discouraged by her experience. To fight the disease, she says, they should

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Can It Get Even Better Than This?

*You don't need to trade in for a newer model—
you can live longer and better...while controlling HIV*

By Charlie Smigelski, RD

At a conference recently, I was having supper with a few of the organizers, who have been living with HIV for over 15 years. I had lectured on nutrition at the meeting, so the conversation drifted to their own concerns. We were talking about having high cholesterol and a “touch of diabetes,” problems that ran in the family for one guy. The other guy had 25 pounds of middle-age gut he kept meaning to do something about. Both mentioned wanting to have a little more energy.

These two were typical of many people at this phase of the disease: some side effects, but not as bad as before, and some body shape changes that were maybe caused by HIV or by HAART (highly active anti-retroviral therapy) or by being 40-something. As we talked about diet and nutrition ideas for them, I recognized a familiar pattern: what they didn't know about good nutrition for long-run health mirrors the situation for most people entering or in middle age; what they didn't know about nutrition for chronic infection and for people on HAART was slowly brewing the fatigue, plus heart disease and diabetes risks. I recognized these as exactly the topics in many medical visits for people these days.

I encouraged my dinner companions to spend some time and energy getting in better nutritional and physical shape. Today, as medicines are doing pretty well with managing HIV, it's time to step back and take stock of the whole person—body, energy, and future metabolic risks. My message for them (and anyone in a similar situation): don't just live with side effects of meds, even though they may be less than before. You might be in okay-enough shape, but imagine having it be even a little better.

What modest changes would it take to feel a little stronger, be in a little better shape, and prevent other complications down the road?

You are what you eat. Think about feeding your body parts just a little better.

Tonight while you sleep, you're repairing brain cells, muscle cells, nerve cells, liver cells, and skin cells. Will your system be sorting through a minefield of groceries to find the right reconstruction materials? Will happy se-

rotonin messages hop through brain cell membranes made of nice slick fish oils, or will the neurotransmitter have to slog through sludgy beef and cheese fat?

Last year, endocrinologist Steve Grinspoon found fatty livers in 50% of people recruited for an HIV metabolism study. A fatty liver is step one in giving people “a touch of diabetes” (especially true for people co-infected with hepatitis C and HIV). Excess weight, antiretrovirals, and oxidative stress of infection play a role in the fat being there, but dietary fats and excess sugar can amplify the problem.

Think about it: what kind of grease was your last serving of French fries cooked in? What kind of semi-plastic shortening was in the muffin or cookies you snacked on yesterday?

The ideal food plan is a caveperson-style diet. It's a chunk of protein for breakfast, and more for lunch and supper. It's careful about fat. For the caveperson, there was only lean protein—fish, mussels, scallops, birds, and maybe deer or antelope. The only other fat to be found back then came from nuts and seeds. The omega 3 oils in fish, plus the oils in nuts and seeds, are the fat your genes are most comfortable with. Corn and vegetable oils are new creations.

The Grinspoon group that reported on the fatty livers also found that people eating more polyunsaturated fats (found in vegetable oils, like corn and safflower) experienced more lipodystrophy. Remember: nuts, seeds and fish oils know how to travel in your system, keeping your face filled out instead of wasting and your arms and legs from looking too veiny/vascular.

For the caveperson, melons, fruits and berries—plus a lot of leaves and shoots—were major fuel sources. Grains hadn't been invented yet, so you would have eaten two bags of spinach leaves to get the 200 calories that Lender stuffs in your bagel. As you can imagine, there is a whole lot more T-cell support in the leaves, blueberries and strawberries than in flour and water, which makes school-kid paste...and bagels.

When you're looking for some starches for dinner, give peas a chance. Dig some tubers, like potatoes. Put some pintos, black beans or lentils on your plate, daily. Okay, after all this, you get some dark chocolate, or milk and a macaroon, for dessert.

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Can It Get Even Better Than This? Continued

The simple truth is this: a higher protein diet with extra big servings of fruit and vegetables, careful selection of fats, and some attention to limiting junk carbs (those muffins and cookies) goes a long way to preventing or reversing lipodystrophy. It also keeps heart disease away.

What kind of metabolic and physiologic shape are you in?

Perform a self-scan, top to bottom, and see what could get buffed up a bit.

Hormones direct your metabolism. How are yours? Be sure your testosterone levels are okay. It's not just about libido—testosterone matters to bone and muscle strength, sugar and cholesterol metabolism, and better mood. When testosterone runs low, the body experiences this condition as something stressful and releases more of a particular inflammatory signal. This messes up insulin signaling and disrupts fat cell refilling. Know what your total and free testosterone levels are. If they are low, fix them. This goes for both men and women.

Ed. note: There is limited data available regarding HIV-positive women and testosterone, but it is known that low testosterone levels can occur. Some physicians replace testosterone in women using patches or gels/creams, though it can be challenging to find a dose low enough to avoid masculinizing side effects like excess hair and acne - careful monitoring is required. There have been promising studies on the impact of testosterone replacement in women to treat muscle wasting; research continues on the impact of testosterone on bones, muscles and energy.

Intestine cells struggle. All stretched out, intestines cover an area the size of a tennis court. Gut cells are replaced every three to four days, a huge amount of work for the body. HIV changes their shape and size, reducing their ability to absorb nutrients. Antiviral medicines, like protease inhibitors, often irritate gut cells.

When something is not right in this gut cell system, it's quite a strain on the body. Gut cells will send out distress signals, but these can distort metabolism, again making it hard to keep fat cells filled up in the right places, and making it hard to maintain weight.

View your intestines as an ecosystem. There are about

4 pounds of beneficial bacteria that live in the intestine. They depend on fruit fibers, like the pectin of apples and bananas, for their nutrition—what they would get from the three to four doses of fruit a day in your caveperson diet. These good bugs make the amino acids and fats that are “repair groceries” for the intestine surface. If they are not doing their job well enough, the back-up amino acid supply for gut repair, L-glutamine, gets pulled from the supply in the muscles. In this way, gut distress and repair problems can affect the muscles all over the body.

In your scan of body systems, think about how your intestines are doing. If you are having diarrhea a few times a week, don't just take anti-diarrhea pills. They only treat the symptom. Behind the scenes, something is not right in the repair process. Use good nutrition as the authentic solution. Eat enough fruit, and then learn about acidophilus/probiotic blends of supplements and L-glutamine to support your gut.

Do you get the diarrhea that happens about one hour after a meal, the “uh-oh, I gotta find a bathroom in about 12 seconds” kind of urge? This is about digestion problems, not about gut cell repair. There is a pH (acidity) problem in your intestines. Protease inhibitors can keep the intestines a little too acidic, so fat digestion is not complete enough. Unabsorbed fat turns to soap, and—bam!—you get the hurry call.

There is a pancreatic enzyme called Pancrecarb (available by prescription) that can help with digestion. Unlike other digestive enzyme supplements, it contains bicarbonate, which helps restore the natural conditions necessary for digestion in the upper intestine. I get emails from people all over the country who tell me that the combination of one teaspoon of L-glutamine powder once or twice a day plus Pancrecarb, taken with meals, has stopped years of diarrhea within a day or two of taking them.

Know what you personally have to do to be sure your intestinal system is in great shape. Your whole body will be happier for it.

Mitochondria are the power plants of cells—they convert nutrients into energy. They are not something you can scan, but your blood fats—triglycerides and cholesterol—can give you a good idea of mitochondrial functional status.

Okay, let's presume that your diet is reasonable and your health status is alright. You eat good foods most of the time, and desserts are modest. T-cells are stable and above, let's say, 100; viral load is less than 20,000. Let's also say you don't eat over-the-top

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Food for Thought

Check credentials before seeking nutritional advice

By Elena C. Blanco, R.D., LDN

Uncovering accurate nutrition information and applying it to daily life can be very challenging in today's world. The media relates story upon story on various nutrition topics, some contradicting each other and some just not making much sense at all. Everywhere you look, you can find different fad diets, new supplements, quick-fix promises, new health foods and celebrities promoting something for weight loss. Food labels are confusing to most people, as are mile-long ingredient lists. Trans fats, organic, aspartame, low-carb and fat-free have become household names.

A proper pedigree

Appropriate nutrition credentials are R.D. and DTR. A registered dietitian (R.D.) is a food and nutrition expert who completed a accepted four-year undergraduate program in nutrition with courses built around biochemistry and physiology. Undergraduate education is followed by at least 900 supervised practice hours approved by the Commission on Dietetic Accreditation of the American Dietetic Association in what is known as a dietetic internship. The internship consists of clinical, food service, long-term care, public health and community rotations. The student then is eligible to be a registered dietitian after passing an intensive examination covering topics from nutrition science to food service management to diseases and conditions that can be impacted by nutrition. Once a dietitian is registered, he or she must maintain their status by taking continuing education courses for credit.

Registered dietitians are working in various settings, including hospitals, long-term care facilities, schools, outpatient centers, doctors' offices, community clinics, government health departments and private practices. R.D.s often have master's degrees or doctorates and can achieve specialties in diabetes, kidney disease, nutrition support (enteral & parenteral feedings) and pediatrics by practicing in the specialty, taking an exam, and maintaining status through continuing education courses. In hospitals, one can find dietitians on every floor, seeing patients based on nutrition risk or through physician consults. They assist patients with everything from teaching them how to eat for their diabetes, to calculating the tube-feeding requirements of someone in an intensive care unit, to making sure a burn victim is getting enough calories and nutrients for healing. They are present with the cancer patients, with the pediatric population, with transplant patients, with those just out of bariatric surgery, and in the dialysis unit.

Registered dietitians also work in the food service end of the hospital, often times being the manager or assistant manager of food service for the entire hospital. Every long-term care facility in the country either has a dietitian on board or has access to one. Dietitians often are found as directors of school food service operations at grade school, high school and university levels. Many nutrition researchers and professors at universities are R.D.s. Many physicians have a dietitian in the area to refer patients to and some even rent out space to dietitians to counsel patients in their practice. Dietitians also work for community-based organizations such as cooperative extensions and Women, Infants and Children (WIC) programs. Government health departments also generally have one or more dietitians on their staff. Dietitians also can be found in their own private practices, counseling patients on weight loss, weight gain, eating disorders, sports nutrition, lowering cholesterol and many other topics.

A dietetic technician, registered (DTR) is a food and nutrition practitioner who completes at least a two-year associate's degree followed by 450 hours of supervised practice experience. DTRs often work in hospital settings assisting dietitians, in long-term care facilities, or in community-based clinics providing nutrition counseling. All R.D.s and DTRs belong to the American Dietetic Association, "the nation's largest organization of food and nutrition professionals."

Finding the help you need

Registered dietitians have spent years trying to gain the recognition that they deserve. It wasn't until 15 or 20 years ago that nutrition was even recognized as a science. Previous to that it was just lumped into home economics. The field of dietetics has come a long way in the past few decades and will likely make huge leaps and bounds in the decades to come.

If you are seeking help or counseling for nutrition, it may be worthwhile to ask them what their credentials are. They may have some good information, but it may not all be correct. And it is important to steer clear of anyone trying to sell vitamins or other herbal supplements out of their offices. True nutrition professionals would not try to sell a supplement to you. We do not promote many herbal supplements because there is not enough data on many of them to warrant us promoting them. One thing to keep in mind is, if you're unsure about the person who is

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Statins: A New Therapy for Hepatitis C?

Liz Highleyman

The publication this summer of a study showing that statin drugs inhibited hepatitis C virus (HCV) replication in laboratory studies generated considerable excitement among HCV positive individuals and their providers. What are statins, and do they represent a new hope for people with HCV?

What are Statins?

Statins, also known as 3-hydroxy-3-methylglutaryl co-enzyme A (HMG-CoA) reductase inhibitors, are approved for the treatment of elevated cholesterol. Low-density lipoprotein (LDL) cholesterol contributes to atherosclerosis (hardening of the arteries), and elevated LDL is associated with an increased risk of cardiovascular disease. A different type of cholesterol, high-density lipoprotein (HDL), exerts a protective effect by transporting fats out of the body.

Statins work by inhibiting an enzyme needed for the production of cholesterol in the liver. In addition to decreasing LDL cholesterol, the drugs also modestly reduce triglyceride levels and raise HDL cholesterol.

The currently marketed statin drugs are:

- atorvastatin (Lipitor)
- fluvastatin (Lescol)
- lovastatin (Mevacor)
- pravastatin (Pravachol)
- simvastatin (Zocor)

With increasing rates of obesity and associated metabolic conditions – both in HCV positive individuals and in the population as a whole – the statins have become one of the most widely prescribed classes of drugs

Statins and HCV

In the July 2006 issue of *Hepatology*, M. Ikeda and colleagues reported on a study showing that certain statins were active against HCV in laboratory cell cultures. Because it is difficult to maintain HCV *in vitro*, the authors developed an HCV RNA replication system, or “replicon,” to evaluate the anti-HCV activity of these drugs.

The researchers found that fluvastatin demonstrated the strongest activity against HCV. Atorvastatin and simvastatin showed intermediate anti-HCV inhibitory

activity, while lovastatin demonstrated only weak activity against the virus. One statin, pravastatin, demonstrated no anti-HCV activity in the laboratory.

The authors also found that when statins were administered with interferon alpha, all except pravastatin exerted an even stronger inhibitory effect on HCV. In the case of fluvastatin, the effect appeared to be synergistic, meaning that the combined effect was greater than the sum of the two drugs considered separately.

The researchers concluded that statins “could be potentially useful as new anti-HCV reagents in combination with interferon.” They noted that fluvastatin plus interferon appeared more effective against HCV than the current standard regimen of pegylated interferon plus ribavirin.

How Do Statins Inhibit HCV?

The reasons for the inhibitory effect of statins on HCV are not well understood. Because all statins work as HMG-CoA reductase inhibitors, the fact that some had minimal or no activity against HCV suggests the antiviral effect occurs by some other mechanism.

In addition, statins did not kill host liver cells, indicating that the anti-HCV activity was not due to cytotoxicity. The researchers suggested that “statins possess the ability to inhibit the replication of HCV RNA via a specific antiviral mechanism.”

Because the antiviral activity of statins was reversed by adding them to the cell cultures mevalonate or geranylgeraniol (two compounds that play a role in the HMG-CoA reductase biosynthesis pathway), the authors suggested that inhibition of these proteins might somehow interfere with HCV replication.

Statin Safety

Though statins are widely prescribed, they are not free of side effects and risks. One of these is the potential for liver toxicity (hepatotoxicity). Though statins have not been extensively studied in people with hepatitis C, it is often the case that drugs that have the potential to cause hepatotoxicity are more likely to do so in patients with pre-existing liver disease.

One recent study, however, found that statins did not appear to increase the risk for hepatotoxicity in patients with hepatitis C.

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HealthWise: Healthy Living with HCV Series Part 4

Tipping the Scales towards Successful Weight Loss

Lucinda K. Porter, RN

Last month's Healthwise column discussed the importance of maintaining a healthy weight, especially for those with liver disease. This month's column focuses on weight loss. We will offer some concrete suggestions for how to make small, but potentially life-saving changes. Throw the word *diet* out of your vocabulary. Skip deprivation. It is possible to lose weight and enjoy life at the same time.

Although it does not have to be torture, losing weight does take thought and commitment. You are more likely to succeed if you formulate a plan. "Failing to plan is planning to fail," notes Pamela Peeke, MD, Assistant Clinical Professor of Medicine at the University of Maryland School of Medicine. Some find it easier to maintain the commitment if there is a plan in place. Hunger and temptation are harder to resist when there is no plan in place.

The most successful weight loss plans encourage a low fat, reduced-calorie diet along with exercise and eating behavioral changes. Ask your medical provider to recommend a weight loss and exercise plan. You may have specific health issues that will need medical monitoring while you are changing your eating and activity styles.

The "trick" to weight loss is this: burn more calories than you eat. It is important to know how much to eat and how much to exercise. Some plans count calories, while others use points or other systems. It takes about 3500 calories to gain one pound of body weight. In order to lose a pound, you need to reduce the amount of calories you eat and/or burn more calories. Unless you are an elite athlete, it is hard to burn that many calories. The best way to approach this is to eat less and move more.

For instance, if it takes 2000 calories per day for you to maintain your current weight, then if you cut back to 1500 calories daily, then in seven days you will lose one pound. In other words, 500 calories a day for seven days equals 3500 calories – the amount you ate to gain that pound. If in the same week you increase your daily exercise by 200 calories daily, then your net loss will be 700 calories per day. You will lose that pound in five days rather than seven.

Personally, I favor the slow and steady method. If I need to lose weight, I will cut back by 200 to 300 calories a day and increase my physical activity. It will not get quick results, but it works. I adapt more easily to small

changes and these are more likely to become permanent ones. Some people are successful with bigger changes, so it may help to identify your style of change.

Two important components of weight loss involve *what* and *how much* you eat. For example, a fish filet sandwich at McDonald's has 410 calories per serving. A regular hamburger has 260 calories. That is a difference of 150 calories. If you dine daily at McDonald's, theoretically you could lose a pound in less than a month just by switching to the lower calorie burger. A large order of fries contains 520 calories, whereas there are 230 calories in a small. Again, if you are a McDonald's regular already, in twelve days you could knock off another pound if you ate the small order instead.

Naturally, a constant diet of McDonald's is not healthy. Fast food can be high in fat and sodium, while low in fiber. Fortunately, many fast-food restaurants offer salads and other healthy choices. The point is, know what you are eating and watch the amounts.

Another concept to keep in mind, is serving size. The label on a small frozen quiche may claim 350 calories. That does not seem too bad except that the label also states there are two servings per container. If you eat the entire quiche, you consume 700 calories.

Choose a food plan that you can stick to. You may have to modify a food plan to include foods that you really want to eat. If you must eat jellybeans every day, then perhaps you can limit your intake to 25 jellybeans a day. This is about 100 calories. You may skip the tablespoon of butter on your morning toast in order to allow for the jellybean calories. However, if jellybeans are a binge food and you can't eat just 25 of them, then perhaps keep them out of the house or only purchase them occasionally and in small amounts.

The National Weight Control Registry maintains a database of over 5000 people who have lost 30 or more pounds and kept it off for at least a year. Here are some of the common practices used by successful weight losers:

- Ate breakfast every day
- Consumed between 1300 and 1500 calories per day
- Weighed themselves regularly and often – either daily or weekly

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Tipping the Scales towards Successful Weight Loss—continued

- Exercised between 60 and 90 minutes of moderate-intensity on a daily basis

If you relapse into old behaviors, it is a good idea to have a good relapse strategy. Refrain from self-criticism. Remind yourself that you are a work in process. Applaud any effort you have made.

To help me meet my goals of healthy eating, I have posted this Turkish proverb at my kitchen table: "He who keeps eating after his stomach is full, digs his grave with his teeth." I remind myself that nothing tastes as good as feeling healthy feels. A piece of cake may look good, but eaten over time it won't feel good. If I think of it in those terms, the choice between food and feeling good is an easy one to make. Furthermore, anytime I contribute to my overall health, I may be keeping ahead of hepatitis C.

Resources

HCSP and the author do not endorse the products or advertising on any of these websites.

For more information, look under the *Resource* sections of previous "Healthy Living with HCV Series" *Healthwise* columns, or check out our new HCSP Guide: [A Guide to Healthy Living with HCV](#).

CaloriesPerHour – caloriesperhour.com This website is a favorite. Start here and you may find everything you need to develop a good weight loss strategy.

Cyberdiet – www.cyberdiet.com This website charges a fee for membership but also offers free information. The Nutrition Calculator is one of this site's many good features.

Diet Detective – www.dietdetective.com This for-profit website offers excellent free information.

Dietwatch – www.dietwatch.com This commercial website maintains the Cyberdiet website. There is ample free information worth looking into, particularly about the emotional aspect of overeating.

The National Weight Control Registry – www.nwcr.ws A national database of over 5000 people who have lost 30 or more pounds and kept it off for at least one year.

Prevention Magazine – www.prevention.com This is an excellent magazine with a helpful website if you ig-

nore the advertising. Check out the following sections: Weight Loss, Food and Nutrition, Fitness to kick off your weight management program.

Overeaters Anonymous – www.aa.org This non-profit program addresses the compulsive nature of overeating by using many of the tools developed by Alcoholics Anonymous.

ShapeUp – www.shapeup.org This nonprofit organization offers excellent practical information.

Three Fat Chicks – www.3fatchicks.com In 1997 these three sisters addressed their collective weight problems by starting this website. If you need support, this is a good place to start.

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"The Fighter Within"

One of our Technical Reviewers informed us of a short HIV/AIDS article with the above title in *The Economist*, November 11, 2006, page 90. The article describes results summarized as "Gene therapy shows some early promise." The article cites results published in "this week's issue of the *Proceedings of the National Academy of Sciences*."

The Economist article stated: "The idea of gene-therapy treatment for HIV/AIDS would be to create a gene that, when placed in an infected person, would make all of the offspring of the cell into which it was inserted resistant to the virus. Even if the virus continued to destroy the patient's immune cells, new ones that could not be infected would replace them. Eventually, the disease would no longer threaten the health of the patient."

The article states that a first step has been conducted at the University of Pennsylvania and VIRXSYS (a biotechnology firm near Baltimore.) Their work consisted of removing immune cells from infected people and replacing them with cells that had been modified to resist the virus.

According to *The Economist*, five infected patients, non-responders to conventional antiretroviral drugs, had their "helper T-cells" removed and treated the cells with an altered form of HIV. "The genetic fiddling disrupted the reproduction of the virus inside infected cells." "According to Carl June of the University of Pennsylvania, their immune systems responded 'as if they were on a vaccine' and it appeared as though their bodies were 'vaccinating themselves' against HIV."

New HCV Antivirals and Drug Resistance

Alan Franciscus, Editor-in-Chief
Lucinda Porter, RN

Researchers are investigating new antiviral medications to treat hepatitis C virus infection (HCV). Some of these drugs are referred to as *direct* antiviral medications since they specifically target HCV. However, unlike current HCV medications, direct antivirals carry the potential for drug resistance. This article will discuss the basics of HCV replication and drug resistance.

The Basics

Viruses are like rabbits; what they do best is multiply. The term for this is *viral replication*. However, a virus cannot survive on its own. It can only survive inside of another living cell, known as a *host cell*. Viruses use various pieces of the host cell's genetic material in order to reproduce. Viruses survive because of their ability to adapt and change when they are under attack from the immune system. Viruses still try to reproduce even while under attack. In a hurry to escape, a virus may make a bad copy of itself, which slightly alters its genetic makeup. The process of change actually produces a variation in the virus, known as a *mutation or quasi-species*.

HCV acts like this. When you are initially infected, your immune system recognizes that an uninvited intruder (HCV) is in your body. Your immune system alerts your body to destroy HCV. However, HCV hurries to escape, makes a sloppy copy of itself, which outwits your immune system. Your immune system is patrolling for the original intruder, not realizing that the virus now looks a bit different. Now HCV can multiply at a faster rate. Eventually your immune system catches on and looks for the bad copy. In a hurry, HCV mutates again. This process may cycle through many mutations.

One way to think about this is with Darwin's theory of evolution and *survival of the fittest*. In nature, the strong survive. The weak die and if they die before they reproduce, their weak genetic material dies too. In this way, it is more likely that strong genetic material is passed along. Evolution applies to plants, animals *and* microorganisms.

Current Therapies

The current standard of care for treating hepatitis C is a combination of pegylated interferon plus ribavirin therapy. How pegylated interferon works is not completely understood. What is known is this: 1) interferon boosts the ability of the body's immune system to kill a virus, and 2) it protects non-infected cells from becoming in-

fectured. Interferon is used to treat a variety of diseases including hepatitis C.

We also do not understand ribavirin's mechanism of action against HCV, but when used with interferon, it seems to interfere with HCV's ability to replicate. Ribavirin alone is not effective against hepatitis C. When interferon and ribavirin are combined, there is a *synergistic effect*, which eliminates HCV in about half the people who take this combination. *Synergy* means that the combined total is greater than the sum of the separate parts.

Drug resistance does not develop with interferon and ribavirin since these drugs do not specifically target the enzymes used in the viral replication process. This means that treatment durations may vary in length and be tailored to patients' needs. Patients may also undergo multiple treatments using the same drug(s). It is also the reason why people may interrupt or stop therapy without the development of drug resistance.

The HCV Replication Process and Direct Antivirals

The hepatitis C virus is a single stranded RNA virus of the *flavivirus* family with a very rapid turnover rate. HCV enters the body and targets the liver – the main replication site of HCV. The virus attaches itself to the outer coating of the liver cell or *hepatocyte*, and enters the cell. After entering the cell, HCV releases its genetic material and hijacks the cell's internal processes.

Now that HCV has taken over, it binds to various *ribosome* sites within the cell. A ribosome is like a factory with printing presses. If a master copy of a document has a mistake in it, all of the copies will have that same mistake. This is referred to as *translation*. Drugs are being developed to interfere with this process, but so far, none has been found to be effective in stopping the translation process.

The next step involves an enzyme called the *protease*. HCV genetic material uses the protease enzyme to 'cut up' the genetic material into smaller pieces before additional viral processing. If this process is interrupted, then the virus cannot make copies of itself. Protease inhibitors are exciting prospects in drug development to treat HCV. Two drugs that look the most promising are VX-950 and SCH 503034.

Other materials that viruses depend on for replication are *polymerase* enzymes. HCV cannot multiply without

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New HCV Antivirals and Drug Resistance continued

these enzymes. Polymerase inhibitors are drugs used to stop this process. The polymerase inhibitor that is farthest along in development in this class is NM 283.

Viral replication relies on the *helicase* enzyme to complete the process. There are no HCV helicase inhibitors currently in development. Most experts believe that it will be difficult, if not impossible, to develop helicase inhibitors.

Resistance and Direct Antivirals

The new direct antivirals work by inhibiting the entry of the virus or by inhibiting the specific enzymes during one of the replication processes. The medications that look the most promising are the HCV protease and polymerase inhibitors. During the normal lifecycle of HCV, the body's immune system exerts pressure on the replicating virus. This pressure produces mutations that escape the host's immune response.

In a similar way, drugs to treat hepatitis C will exert pressure on the virus to change and mutate in order to survive. For this reason, it is believed that most of the direct antiviral medications will produce drug resistant mutations, especially if these drugs are taken for a long time. This in turn may make the new medications ineffective in treating the new viral mutations.

Drug resistance is inevitable. However, scientists are looking for ways to prevent or interfere with drug resistance. For instance, drug resistant mutations may be identified earlier in the process, such as during the test tube development phase.

Preventing and Reducing Drug Resistance

The reduction or prevention of drug resistance depends on a number of factors. Some of these are:

Eradicating HCV: Unlike HIV and HBV, hepatitis C does not integrate into the host cell. For this reason, we have been able to eradicate HCV from the body with the use of current medications – pegylated interferon and ribavirin. In addition, HCV is an RNA virus. Since it does not integrate into the host cell's DNA it will be easier to eliminate HCV without the risk of viral mutation.

Combination of direct and indirect antivirals: Direct antivirals can be given for a shorter period of time, thus

reducing drug resistance. When used in combination with indirect antivirals – peginterferon and/or ribavirin, the risk of resistance drops. An example of this is extending the duration of treatment with peginterferon and/or ribavirin after stopping the direct antiviral. This may prevent drug resistance while allowing for continual viral suppression. For instance, a new clinical trial of VX-950 is underway to test the theory of taking VX-950 for 12 weeks with and without pegylated interferon, followed by additional treatment using just pegylated interferon with or without ribavirin. Hopefully, this trial will test this theory and more importantly, find out if taking this new antiviral results in a durable sustained virological response.

Potent direct antivirals: The development of potent direct antivirals that quickly distribute throughout the body and reach high blood concentrations in a short time period will exert enough pressure on the virus before it has a chance to mutate. If the drugs are not potent enough, the escaped viral mutations may become the dominant virus, rendering the antiviral medication ineffective.

Combination direct antivirals: The use of direct antivirals that inhibit several different protease and/or polymerase enzymes simultaneously, will reduce the ability of the virus to mutate.

Adherence: Current HCV medications require adherence to prescribed doses and durations to be more effective in treating HCV. The new direct antivirals will require strict adherence. Doses that are skipped or forgotten could lead to viral mutations and drug resistance.

HCV research has benefited from what we know about HIV and HBV drug resistance and hopefully will be able to contribute to this body of knowledge. As we begin this era of new HCV medications, now is the right time to develop strategies to make HCV therapy more effective. Now is the time to reduce the chances of the emergence of drug resistance that could potentially negate some of the benefits of new therapies. The best strategy for moving forward depends on using knowledge from the past in order to discover the future.

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HealthWise: Dietary Supplements

Lucinda K. Porter, RN

Let us start with a “what if” game. If you are not feeling well, then you are especially ready for this game. If you are feeling well, try to remember a time when you felt lousy. What if someone tells you that you will feel better if you try one of the following: a vitamin or supplement, a prescription medication, a diet, an exercise program or going to bed earlier. Which would you choose?

If you are like me, you picked the vitamin or supplement. My natural inclination is to take the path that I perceive to be easiest and most pain-free. I do not like to take medication, particularly if the side-effect risk is high. Diet and exercise are uncomfortable. My life is full and I would much rather take a vitamin than get a decent night's rest.

However, health is not a game. I told you how I would play the game but this is not how I live my life. Most of the time, I take the uncomfortable path – the one I resist. Diet, exercise and sleep are at the top of my list. Recreation, stress reduction and spiritual practice are also at the top of my list.

I do not expect to find health in bottles. I treat dietary supplements with the same respect as I do medications. I consult with my doctor. I do my homework. I understand the potential risks and benefits. I use them when I need them. I am grateful that supplements are available.

Patients frequently ask me what I take. The reply is complicated, depending on a number of factors. In this month's column, I will discuss some of the guidelines I use when choosing a vitamin or mineral. Please note that these are **my** guidelines and not necessarily those of *The HCV Advocate*. My goal is not to give advice but to stimulate thinking about your health, while providing tools to enable you to make solid decisions. I am not an expert in this area. Always consult with your medical provider and other experts before taking any drug or supplement.

Start with the experts: Discuss dietary supplements with your medical provider. If your provider does not know much about supplements, ask for a referral to an expert. Even if your provider knows little on the subject, if he or she is willing or open-minded, the two of you can learn together. No one should ever belittle or dismiss you because of this interest.

Tell your provider about everything you are taking: Some supplements interact with medications and other supplements. For instance, patients taking Coumadin (warfarin) or other blood thinners should avoid vitamin K unless advised otherwise. The Internet provides tools that

will check for interactions between everything you are taking. The *Resource* section at the end of this column lists sites with this information.

Find good information: I subscribe to a number of publications. The *Nutrition Action Health Letter* is my favorite. If you can afford it, this organization is worthy of financial support. You can access portions of the newsletter on line or at your public library.

I support services and organizations that promote research and better industrial practices. For instance, ConsumerLab.com provides independent lab testing for dietary supplements. Manufacturers voluntarily submit products. Products that meet or exceed certain standards, are allowed to carry the of ConsumerLab seal of approval. I check the ConsumerLab list before purchasing a dietary supplement.

Know what to buy: Buy products that submit to voluntary self-regulation. Supplements that strive to meet standards show that the manufacturers put extra effort into their products. There are a variety of insignias, designations and “seals of approval.” Some are The United States Pharmacopoeia (USP), NF, NSF, and ConsumerLab.com (CL). Standards have also been set by Germany's Commission E, the British Herbal Compendium, the World Health Organization, the American Herbal Pharmacopoeia, the American Herbal Products Association and others. Products that followed GMP - “good manufacturing practices” - suggests more effort went into manufacturing. (In Canada, the GMP means “good manufacturing process.”)

Supplement with food: Our bodies utilize vitamins and minerals from food sources. Good nutrition is the foundation for vitamins and minerals. Do not use supplements as a substitute for good nutrition.

More is not better: In fact, high doses of some vitamins may be harmful. In particular, avoid high doses of vitamin A. Aim for no more than 4000 International Units (IU)ⁱ daily of retinol (a form of vitamin A) or 15,000 IU of beta-carotene (a form of vitamin A). To be safe, keep vitamin E to 100 IU.ⁱⁱ The daily value of zinc for women is 8 mg, and for men it is 11 mg – never exceed 23 mg of zinc.ⁱⁱⁱ Avoid high doses of vitamin B-3 (niacin) and take no more than 100 mg of vitamin B-6.^{iv} Keep phosphorous and magnesium to less than 350 mg.^v

Less may not be enough: Choose a multivitamin that contains at least the minimum Daily Value (DV). Look for a multi that has at least 50 mcg of selenium and at

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Dietary Supplements continued

least 10 mcg of vitamin K (50 mcg for men and women under 50).^{vi}

Multivitamin-Mineral Supplement: Unless your medical provider advises you otherwise, look for a multivitamin with no or low iron. "Senior" or "over 50" versions of most major brands are usually low or without iron. Choose a multi that has at least 100% of the Daily Value (DV) for vitamins B-1 (thiamin), B-2 (riboflavin), B-3 (niacin), B-6, B-9 (folic acid), B-12, C, D, E. The very best multis have at least 10 mcg of vitamin K, 35 mcg of chromium, and no less than 11 mg or more than 23 mg of zinc.^{vii}

Iron: Liver patients should not take additional iron without consulting their medical providers. Iron dosages depend on many factors, including gender, age, diet, and health history.

Calcium and Magnesium: The recommended dosage of calcium depends on individual factors, such as age, gender and health history. Optimal doses of magnesium start at 100 mg; do not exceed 350 mg.^{viii} Calcium and magnesium are bulky, so it is best to supplement these separately from a multivitamin.

References:

^{i-viii} *The Multivitamin Maze*, Nutrition Action Health Letter March 2006

Resources

* Center for Science in the public Interest www.cspinet.org This nonprofit lobby group is a leader in the nutrition and food safety arenas. They publish the *Nutrition Action Health Letter*.

* The Cochrane Collaboration www.cochrane.org Independent and reliable review of medical evidence.

* ConsumerLab.com www.consumerlab.com Independent, reliable testing of supplements voluntarily submitted for analysis. Some free information, but there is a membership fee to use all of this website's resources.

* Drugs.com www.drugs.com One of the many fine features of this website is the drug interaction tool. Use this to check for potential interactions between drugs and supplements.

* Mayo Clinic www.mayoclinic.com

* Memorial Sloan-Kettering Cancer Center www.mskcc.org/mskcc/html/11570.cfm

* National Institutes of Health Office of Dietary Supplements www.ods.od.nih.gov/Health_Information/Health_Information.aspx

* Supplement Quality www.supplementquality.com Information about supplement safety and how to read labels.

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Statins: A New Therapy for HCV? Continued

S. Khorashadi and colleagues assessed the incidence of liver toxicity in 166 HCV positive patients treated with statins, 332 HCV positive people not receiving statins, and 332 HCV negative individuals taking the drugs. They found that among HCV positive individuals, use of statins was associated with a higher rate of mild-to-moderate liver biochemistry elevations compared with those not on statins (23% vs 13%, respectively), but a lower incidence of severe liver enzyme elevations (1% vs 7%).

Among patients started on statins, the rates of mild-to-moderate elevations were similar in subjects with and without HCV (23% vs 16%, respectively). HCV positive and negative patients also had similar rates of severe elevations and statin discontinuation due to hepatotoxicity. The authors concluded that "[s]tatin therapy was not associated with a higher risk of severe hepatotoxicity in patients with chronic hepatitis C and appeared safe."

For HIV/HCV coinfecting individuals, an additional concern is the potential for interactions between statins and antiretroviral drugs, particularly protease inhibitors, which could alter drug levels in the body.

Looking to the Future

HCV positive people have already begun asking whether statins might play a role in hepatitis C treatment. Research on this class of drugs as antiviral therapy is still in the preclinical stage, and it will be some time before human clinical trials show whether statins are effective for this indication. In the United States, however, clinicians may prescribe medications "off-label" for indications other than that for which the drugs were approved.

The latest data suggests that statins may one day become a component of combination therapy for chronic hepatitis C, and that the drugs appear to have an acceptably low level of hepatotoxicity in people with HCV. While we await the results of further research, HCV positive individuals who are already taking statins to reduce their cholesterol may be deriving an additional, unexpected benefit.

References

Ikeda, M. et al. Different anti-HCV profiles of statins and their potential for combination therapy with interferon. *Hepatology* 44 (1): 117-125. July 2006.

Khorashadi, S. et al. Incidence of statin hepatotoxicity in patients with hepatitis C. *Clinical Gastroenterology & Hepatology* 4 (7): 902-907. July 2006.

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The 10-Point Inspection, HIV-Style: What to Check Under the Hood

Some of the most important tests, and what they mean

By Judith Feinberg, MD

In many parts of the world, medical providers care for their patients who have HIV/AIDS without the benefit of laboratory tests—sometimes even the most basic ones. Fortunately, in the United States (and various other countries), medical providers almost always have available to them a wide range of diagnostic tools. Below are ten (plus three) of the most important ones.

1. Complete blood count (CBC).

This tells you whether you are anemic (too few red blood cells), neutropenic (too few of the white blood cells called neutrophils that fight bacterial infections) or thrombocytopenic (too few platelets, or thrombocytes, for your blood to clot normally)—all of which occur commonly in people with HIV. The CBC also gives you something called the “differential,” which is an individual count of all the different kinds of white blood cells: neutrophils, monocytes, lymphocytes, basophils, and eosinophils. It is also crucial to determining your total CD4 (T4, T helper) cell count, a critical measure of immune function.

2. CD4 cell count.

The FACS (not “fax,” although pronounced the same way) or Fluorescence Activated Cell Sorter machine identifies CD4 cells and directly measures what their proportion (percent) is of all your lymphocytes (white blood cells) when your blood was drawn. So, the CD4 percent is what the machine actually measures, and the total (or “absolute”) CD4 cell count is derived from multiplying the percentage of CD4 by the total lymphocyte count. That is why the differential (see above) from the CBC is necessary—in order to obtain your CD4 cell count.

Over time, the CD4 percent is a more stable measure of your immune system function because the total CD4 count is influenced by your white blood cell count at the moment your blood was drawn, a number that varies constantly. Nonetheless, by habit and tradition, health care providers have used the total CD4 cell count for key decisions, such as starting HIV meds or preventive therapy for opportunistic infections, like PCP (*Pneumocystis pneumonia*).

3. HIV RNA PCR (HIV ribonucleic acid poly-

merase chain reaction), or “viral load.”

This key test tells us how much virus is in a milliliter (abbreviation: ml) of your blood, one-fifth of a teaspoon. Note that it does not tell us how much HIV is in your entire body, where most of the virus is—in tissues, such as your lymph glands (lymph nodes). Even though this test uses a tiny quantity of blood, it has proven to be a very good indicator of response to antiretroviral therapy.

There are two versions of the most commonly used test, the Roche assay, and both have established cut-off values for the upper limit of how much virus can be detected and the lower limit, which is referred to as “undetectable” virus. Note that “undetectable” means the amount of HIV is less than the technical ability of the test to detect it and does not mean that HIV is not present.

The Amplicor version of the viral load assay has a low end cut-off of “less than 400 copies/ml” of HIV RNA/ml and an upper limit of “greater than 750,000 copies/ml.” The Ultrasensitive test has a low end cut-off of “less than 50 copies of HIV RNA/ml” and an upper limit of “greater than 75,000 copies/ml.” The significance of the difference between these two tests is that the Amplicor test is more accurate at higher viral loads and the Ultrasensitive test is more accurate at the low end of viral loads.

It is useful to do the Amplicor test when someone is first evaluated for HIV disease because it is valuable to know before starting treatment if the viral load is in the thousands, hundreds of thousands, or millions. Once someone is on HIV treatment and is doing well, it is more useful to use the Ultrasensitive test, given that the goal is to get the viral load as low as possible and this test is able to detect lower levels of virus in the blood.

There are other types of viral load tests, such as the branched DNA (bDNA) assay, that are sometimes used. There are various technologies but the measurement principles, with cut-offs for the upper and lower limits, are similar to what is described for the RNA PCR tests above.

4. Serum Chemistries—liver and kidney function tests.

Liver Function Tests (LFTs):

These tests measure some key functions of the liver, a

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The 10-Point Inspection continued

complex organ that does many important tasks in the body. The liver manufactures proteins that are essential to blood-clotting and to keeping fluid in your bloodstream instead of leaking out into your tissues and causing swelling (edema). The liver breaks down most environmental poisons (toxins) and drugs to rid the body of them. It also forms bile, which is important for digestion.

Amino aspartate transaminase (AST, formerly SGOT) and alanine aspartate transaminase (ALT, formerly SGPT) are key enzymes that indicate how well liver cells (hepatocytes) are functioning. The levels of an enzyme called alkaline phosphatase and a protein by-product called bilirubin indicate how well the production and excretion of bile is going. Albumin, a protein made in the liver, is critical for keeping fluid in the bloodstream and is an overall measure of nutritional status.

Liver function can be damaged by alcohol abuse, environmental toxins (including street drugs), viral infection of the liver (viral hepatitis) and a long list of diseases. Since people with HIV sometimes also have chronic hepatitis B or C, drink too much, or experience liver damage (hepatotoxicity) from medications, LFTs are important to monitor.

Kidney (renal) function tests: These tests measure how well your kidneys are doing their primary job, which is to rid the body of protein waste (blood urea nitrogen, or BUN) and regulate blood volume by filtering out the waste and extra water to form urine. The two main kidney function tests look at the level of waste as a way to measure how efficiently your kidneys are operating. These tests can provide clues that someone might have HIV-associated nephropathy (HIVAN) or kidney malfunction due to other causes, such as dehydration or drug toxicity.

Since some drugs are excreted from the body by the kidneys, dose adjustments need to be made when a person develops altered kidney function. Awareness of kidney dysfunction is also important when selecting an ARV regimen because some medications, like Viread, are not preferred for someone with underlying kidney disease.

Kidney function should be checked when someone enters HIV care. Thereafter, people at high risk of developing kidney disease (primarily African Americans and diabetics or people with a family history of diabetes) should have their kidney function checked at regular intervals. Routine checks are also recommended for people on ARV therapy.

5. Syphilis blood test.

Syphilis, like HIV, is a sexually transmitted infection that may have no symptoms at all. If left untreated, it can cause—years later—significant disease and death due to damage to blood vessels and the brain.

There are a number of blood tests for syphilis (RPR, FTA, syphilis IgG), but the type of test is less important than the fact that everyone with HIV should have one upon entering HIV care and women who become pregnant should have one. After that, screening depends on risk—people who are at higher risk of exposure through unprotected sex, especially with multiple partners, may need to be screened regularly. Several outbreaks around the country among men who have sex with men have occurred over the past several years. Sex workers, incarcerated individuals, and people with other sexually transmitted infections are also at high risk.

6. Tests for viral hepatitis.

Many HIV-positive people are also infected (“co-infected”) with chronic hepatitis B virus (HBV) and/or hepatitis C virus (HCV). It is very important to find this out because, if left untreated, both conditions can ultimately lead to severe scarring of the liver (cirrhosis), liver failure, and liver cancer (hepatocellular carcinoma, or HCC for short).

Some HIV medicines are active against hepatitis B, so it is important to craft an ARV regimen that will adequately treat both HIV and HBV at the same time. Hepatitis C currently requires treatment with two drugs that do not control HIV, and this therapy can be pretty challenging. However, depending on virus type and other factors, treatment can be very effective.

In addition to HBV and HCV, it is also important to test your blood for proteins that are protective (called antibodies) to hepatitis A (HAV). There is no chronic form of hepatitis A, but if you already have chronic liver disease from hepatitis B or C, you can get much sicker from hepatitis A than someone who doesn't have HBV or HCV because you already have some liver damage. Since there are vaccines available for hepatitis A and B (but not, unfortunately, for hepatitis C), these should be offered to every HIV-positive person whose blood tests show no prior exposure to these viruses.

7. Resistance tests (genotype & phenotype).

These tests tell us whether your virus is resistant to certain HIV drugs (in other words, the medication is not effective against your virus). Testing for transmitted resistance is now recommended before starting HIV meds, as up to 16% of people have a virus that is resistant to one or more antiretrovirals. These tests are also crucial for people who are not responding to their HIV therapy.

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Both genotypes and phenotypes are done on a blood sample. Genotypes, which are simpler, faster, and cheaper to perform, identify changes in particular viral genes that are associated with reduced or no response to specific drugs. Phenotypes, which are more complicated, time-consuming, and expensive to perform, test how well your HIV grows in the presence of different concentrations of HIV drugs.

Genotypes may be more than adequate for early resistance because they look at how much resistance the virus has compared to virus with no resistance; phenotypes have some advantages for people with extensive resistance because they can indicate how well the virus responds to individual drugs. The phenotype results can be especially useful when there are no “new” drugs available to someone and the only option is a “salvage” regimen of drugs to which the virus is still susceptible.

In the most difficult cases, both tests add information of value. Cost can limit the availability of these tests, especially the phenotype.

Additional tests, when a closer inspection is warranted

1. Testosterone level.

Among other key functions, testosterone is the hormone that drives sexual interest (libido) in both men and women, though normal levels for women are much lower than for men. Symptoms of low testosterone (hypogonadism) in men include: depression, lack of energy, reduced muscle mass, and decreased sex drive or arousal. Much less is known about women and testosterone, but low testosterone levels in women also cause decreased sex drive.

Hypogonadism seems to be common in HIV-positive men, though it is not known why. Testosterone levels in men normally decline with age, so the level has to be interpreted with your age in mind.

Testosterone replacement can be done by injection every few weeks or by gels or patches that are applied to the skin every morning. It is difficult to replace testosterone in women because the amount needed is so small, and current doses of various testosterone preparations are geared for treating men.

2. Thyroid hormone level.

Low levels of thyroid hormone (hypothyroidism) are reasonably common in women—HIV-positive or not. Low thyroid levels can cause weight gain, lack of energy, depression, and skin changes. A thyroid stimulating hormone (TSH) level can screen for an underactive, as well as overactive, thyroid gland. Both underactive and overactive thyroid conditions can be treated.

3. DEXA (dual X-ray absorptometry) scan.

This scan tells us about the composition of the vari-

ous body compartments—bone, fat, muscle—and is particularly useful in determining whether you have lost a modest amount (osteopenia) or too much (osteoporosis) of your bone mineral content. Osteopenia and osteoporosis weaken your bones and make them prone to breaking (fractures).

Bone mineral loss can occur in men with low testosterone levels and women who have stopped having periods (menopause). It can also run in families. This problem can largely be avoided with a good intake of calcium (at least 500 mg per day in dairy foods and leafy greens or as a supplement) and vitamin D (from exposure to sunshine, in fortified milk, or as a daily supplement).

It is important to do the kind of exercise that makes your muscles tug on your bones, such as resistance exercises that use weights or elastic bands. Walking briskly several times a week is also helpful because you are bearing your own weight, which helps keep your bones strong. In addition to calcium, vitamin D, and exercise, you can treat severe bone mineral loss with a medication you take once a week or once a month to help reverse bone loss.

Note: DEXA scans can also measure how much fat you have inside your body (visceral fat) and under your skin (subcutaneous fat), although this is more of a tool in studies of fat gain and loss (lipodystrophy) than a test used in the clinic to help with treatment of your HIV disease.

8. Serum lipids.

Diet, exercise, cigarettes and your genetic heritage (the genes you inherited from your parents and ancestors) all influence your risk for heart disease. Since we now expect HIV-positive people to live a long time, we have to pay attention to the fact that both HIV itself and some of the medications used to treat it have been associated with abnormal lipid levels (cholesterol and triglycerides, which are fats in the blood). This makes it important to obtain fasting lipids when you first enter HIV care, and to have them repeated at least once a year. Repeating them more often will depend on whether they are normal or not to begin with and what other heart disease risks you have—are you overweight? Do you smoke? Do you have diabetes or high blood pressure? Do you exercise? Do you have a family history of high cholesterol or heart disease?

To be accurate, lipid testing must be done in the “fasted” state—no food (or drink, except water or diet soda or plain tea or black coffee—any drink without calories) for a minimum of eight hours, ideally 10 to 12. Fasting lipids include four separate

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Can It Get Even Better Than This? Continued

amounts of grease and sugar and you don't have fevers and wasting, which can also raise blood triglyceride (fat) levels.

You have probably heard the term "mitochondrial toxicity," especially with respect to drugs like d4T and ddI, which have been shown to cause more mitochondrial damage than some other antiretrovirals. When mitochondria are damaged, fat you eat isn't burned up for energy completely enough and it accumulates in cells. Switching to a less toxic drug can reduce the mitochondrial damage, but repair is slow and fat metabolism is sluggish, and so, are you.

Cells clogged with fat are irritated and release a stress signal that messes up sugar metabolism, including insulin activation. A chronic infection like HIV (or HCV) generates many stray electrons ("those darned free radicals," as Dr. Judy Shabert has called them), which means more mitochondrial stress.

For someone with HIV, a blood triglyceride (think: grease) level above 150 suggests mitochondrial energy-processing trouble. Triglycerides travel with a cholesterol coating, so blood cholesterol levels rise, as well. Unfortunately, the level of "good cholesterol," HDL (high density lipoprotein), doesn't rise amid the irritation—it drops.

It is common to treat the high lipids with a statin drug like Lipitor, or a fibrate like Tricor, but these are seldom effective enough. Medical groups at the VA and at Baylor University report that 75–80% of their HIV patients with hyperlipidemia fail to reach proper cholesterol and triglyceride lipid levels using standard drug treatments. While statins and fibrates lower blood fats by blocking an enzyme that's needed to make cholesterol, nutrition repairs the basic cellular problems of mitochondrial distress, poor fat-burning, and deranged sugar metabolism.

Be nice to your mitochondria

When it comes to mitochondria, what my recent dinner friends and you need to know is how to help liver and muscle mitochondria restore fat-burning and energy-making ability.

First, taking some extra antioxidants, like 1,000 mg of vitamin C and 600 IU of vitamin E each day, can go a long way to repairing mitochondria. Next, taking 1 to 1.5 grams a day of the amino acid L-carnitine for a month or two can generally lead to a drop in triglyceride levels by at least 25%. Then, taking 3 grams a day of

omega 3 fats (fish oils) tells the liver cells to burn off some stray fat in peroxisomes, alternative energy-making units in cells.

The combination of caveperson diet, two to three antioxidant vitamin pills per day, some fish oils, and L-carnitine for a few months offers the prospect of radical improvement in blood fats. One of my patients on Kaletra and Combivir, plus gemfibrozil to lower lipids, had his triglycerides drop from 1800 to 400 in four weeks after he adopted this nutrition regimen. Another patient, on a PI-only regimen of Kaletra and Fortovase and 10 mg of Lipitor, had a cholesterol of 278 and triglycerides of 1,400. Seven weeks into the caveperson diet plus two antioxidant-with-B-complex vitamin pills, 3 grams of fish oil and 1 gram of L-carnitine, he e-mailed me to report his cholesterol was down to 172 and his triglycerides were at 166. He had also gotten back to a walking program of three to four times a week.

How close is your diet to this list *each day*?

Protein foods: breakfast, lunch, and dinner

Fruit servings: 3-4 times per day

Vegetables: at least 2 cups a day

Carbohydrates that digest slowly (black beans, lentils, peas, corn)

A handful or two of nuts and seeds

Zero fats that harm your body (cream, butter, stick margarine, hydrogenated shortening)

The supplement regimen is not forever. Taking some good vitamins to support both CD4 and CD8 T-cells is fundamental. This can cost as little as \$12 for a six-month supply (e.g. Trader Joe's Vitamin Crusade antioxidant formula). Buyers clubs (e.g., Boston, Houston and New York Buyers Clubs) have more potent combinations that cost more but include more immune-supportive trace minerals, like selenium and magnesium. (Visit www.bostonbuyersclub.com, www.houstonbuyersclub.com, and www.newyorkbuyersclub.org.)

You might take less of the other supplements. Salmon for lunch and supper a few days a week may replace fish oil pills. A lot of people find the L-carnitine gives them energy, so they keep taking some. Some people take 100 mg of coenzyme Q10 for a few weeks at a time, because they feel it also gives them added energy. These extra supplement items each cost \$10-\$15 a month, which adds up. Save money; use them when you need them.

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The 10-Point Inspection continued

measurements of different forms of fats that circulate in your blood: total cholesterol, high-density lipoprotein (HDL, or “good cholesterol”), low-density lipoprotein (LDL, or “bad cholesterol”), and triglycerides.

High levels of HDL protect you against heart disease caused by clogged arteries in your heart (atherosclerotic heart disease). Unfortunately, high levels of the other fats are associated with an increased risk for heart disease. Lipid levels can be lowered with lifestyle changes, but some people may also have to take lipid-lowering drugs in addition to a diet change and other interventions.

9. Pap smear.

A Pap smear involves scraping cells from the cervix or anus (usually with a tiny cotton swab), preparing them on a slide, and viewing them through a microscope. Every HIV-negative woman should be screened once a year for cell changes on the cervix that could lead to cervical cancer. Depending on CD4 count and other factors, women who are HIV-positive should be screened twice a year (every six months) for cervical cancer.

Cervical cancer is caused by infection with certain strains of human papillomavirus (HPV). Cervical cancer is a real threat to HIV-positive women, especially at lower CD4 counts, and became part of the case definition of AIDS in 1993. If caught early, it can be cured.

Anal Pap smears are still not standard of care due to limitations of the test and because an expert is needed to accurately analyze the results. The wealth of data that exists for cervical Pap smears does not exist for anal Paps, so questions remain about its reliability and predictability as a screening tool. In some centers, anal Paps have been an effective way to screen for anal carcinoma, but many centers lack health care providers and pathologists (the doctors who interpret Pap smears) who can perform this test reliably.

This test was developed initially for men who have sex with men, thought to be susceptible to anal carcinoma because of sexually transmitted HPV infection. However, women can also benefit from such a test, even if they have not had anal intercourse.

10. Screening tests for cancer.

Now that HIV-positive people have the prospect of living out a normal lifespan, it is important to provide cancer-screening tests because most cancers are

age-related. Also, there is some evidence that people who are HIV-positive may be at higher risk for a broader range of cancers than the ones that have long been HIV-associated, like Kaposi's sarcoma and B cell lymphoma.

The guidelines for performing these screening tests are the same as those for HIV-negative individuals.

For men aged 40 and older: an annual prostate-specific antigen (PSA) blood test to look for prostate cancer

For women aged 40 and older: a baseline mammogram (type of x-ray) to detect breast cancer, with subsequent mammograms based on age and family history

For all people aged 50 and older: a baseline and then subsequent colonoscopy to detect colon cancer

For smokers: QUIT! A chest Xray may be prudent for smokers, but there is no clear interval for subsequent screening.

Judith Feinberg, MD, is a clinician and Professor of Medicine at the University of Cincinnati, where she is also the Director of the AIDS Clinical Trials Unit. Dr. Feinberg is an American Academy of HIV Medicine (AAHIVM)-credentialed HIV Specialist. Positively Aware, Fall 2006 Special Issue

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Food for Thought continued

counseling you and their expertise, you are likely not seeing a reliable person for the information. Watch out for the “nutritionists” promoting rapid weight loss, extremely low-calorie diets or anything that makes you feel uncomfortable.

If you are interested in finding an R.D. to provide you with accurate nutrition information, check your local hospital. Many hospitals have outpatient dietitians who will counsel you on any topic you may be interested in. You also can check your local yellow pages under dietitian or nutrition to find local private practices. Or you can ask your physician if they know of a dietitian that they refer other patients to. There may be a fee, as many insurance companies still have not recognized how important good nutrition is in our lives. In a country with increasing health problems directly related to nutrition, there is a greater need than ever before for reliable nutrition experts.

Hepatitis Magazine, July-September 2006

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25 Years in the Fight Against AIDS: What Have We Learned? Continued

Leadership within NIAID wisely created a balance of programs that supported basic science about HIV itself, HIV pathogenesis (how HIV causes disease), drug discovery, and clinical testing of new drugs. The funding was spread throughout the country to attract the involvement of our best universities and. The more these groups saw the opportunity for secured long-term funding, working in AIDS became the smart thing to do.

Similar directed funding was used to kick-start the involvement of America's pharmaceutical companies. Federal grants helped identify the basic targets for therapy and supported the screening and testing of new drugs. Within a decade or less, industry had taken the ball and run with it. Smaller and newer firms were seeded with federal grants to do the early work on novel AIDS-related products while the larger companies funded the development of compounds through the costly and time consuming FDA approval process. Today, most HIV drug development is the work of a small cluster of major firms, each heavily invested in developing a full portfolio of products that attack HIV from multiple angles. As treatment has begun to be made more accessible in developing nations, the international generic drug industry has taken on the task to producing less expensive and sometime innovative new versions of existing drugs.

Another key element of the success achieved in treatment has been the unprecedented inclusion of the patient and primary care physician communities into the research process. After years of initial reluctance, patients and their care givers were eventually welcomed into scientific meetings and onto drug company advisory boards. For many years now, every clinical study has been massaged by the patient community, not just institutional review boards and professional groups.

This involvement of an aggressive and well informed patient constituency has been widely heralded by scientists and patients alike. Its contrast with the passive community advisory boards of the past couldn't be more stark. Its contribution to progress and understanding cannot be overstated.

Despite the painfully slow start in the Reagan era, steadily increasing funding of AIDS programs at the NIH orchestrated our academic and industrial resources toward achieving long-term goals. Long-term, consistent funding made it possible for academia and private industry to confidently invest in HIV without worrying when or whether the funding would dry up. Opening the doors of academia and private industry to the voices of those affected by the disease has humanized

the science and brought it new levels of both support and useful constructive criticism. Collectively, these efforts proved that investing heavily and consistently in the fight against a disease and opening the doors to greater public input does indeed pay off. They showed that science can be guided toward specific goals, albeit with a gentle but wise hand. The key to such wisdom has been to bring all the relevant parties to the table and to continually remind ourselves of the importance of the patients' voices.

These efforts have changed HIV disease from a rapidly progressing, almost always fatal condition to what is today a largely manageable condition, at least for those with access to medical care. In this 25th year of AIDS, we have nearly 25 new drugs that have collectively changed the nature of the disease.—an unprecedented rate of new drug development. When people have access to the medicines and medical care, HIV can be held at bay for decades. Though this is not yet a cure, it is a stunning and welcome advance over the suffering that people faced early in the epidemic.

We have also learned the critical importance of combating drug resistance through patient adherence training and developing a constant stream of newer and better drugs, something neither tried nor accomplished very well in any other disease. Developing newer and better drugs continues to this day with at least four or five important new medications nearing approval over the next two years. With each passing year, HIV becomes more manageable, the drugs safer and easier to use, and the development of resistance ever more distant.

If only we could make as much progress against the social, economic and political obstacles faced by people with HIV worldwide. Drug prices, lack of infrastructure, sanitation and medical care, and the callous indifference to the needs of the poor keep many millions from benefiting from these advances. As long as these obstacles remain, these benefits remain out of reach for far too many. We have also failed miserably in the pursuit of prevention, both nationally and internationally. We would not need to struggle so mightily to find the funds to support treatment for tens of millions of people around the world if we had perhaps invested more effectively in prevention along the way. Conversely, had we succeeded in prevention, the cost of treatment would be greatly reduced since fewer people would need treatment in the first place.

We cannot afford to ignore these important lessons. In addition to bringing the success of HIV treatment to the developing world, these lessons should now be applied to the fight against any number of other major illnesses that have not fared as well at the hands of government and science. In the same developing countries so badly

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25 Years in the Fight Against AIDS: What Have We Learned? Continued

in need of access to HIV treatment, millions more die annually from such diseases as tuberculosis, malaria and hepatitis. We cannot go back to serendipity and lower, inconsistent funding levels. We cannot go on underfunding prevention efforts. A vaccine for HIV still tragically eludes us and the vaccine research effort still seems inadequately funded and lacking in leadership. These challenges are as great and as unmet today as they were in the 1980s. Our very success in treatment research and development points the way toward success in prevention: it requires bold, consistent, long-term funding and worldwide collaboration among patients, physicians, researchers, governments and the general public. That is what it took to change the nature of HIV disease through treatment research, and it is what it will take to stop its spread.

Beyond HIV, we face new threats like the bird flu and other less well known pathogens, plus whatever nature will bring us in the future. Thanks to the efforts of scientists, activists, doctors and nurses, the National Institutes of Health, our universities, private industry and supporters in government, we now know a great deal about fighting HIV and any other new disease. The challenge before us now is to apply those lessons worldwide.
PI Perspective #42, October 2006

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Blood Lite continued

take advantage for the treatment options available, but they should keep close tabs on what the powerful drugs are doing to their bodies.

"I would tell people to be prepared for what anemia really means. It means that you may get tired very easily; you may not be able to function as usual. Walking up a flight of stairs or across the room can be extremely exhausting," she says. "A person has to make arrangements to have others help with regular activities. I think it is worth the pain for a few months, if you get the results you want from the treatment."

Lyons says he has to look no farther than the loved ones around him for the source of his perseverance. "All the interferon I have taken over the years has at least bought me time. Even though the quality of life was pretty poor, I was given enough time to raise all my children to adults, and that was worth it even though the treatment was not successful at killing the virus," he says. "I would do it all again – without a second thought – for the chance to raise my children."

Hepatitis Magazine, April-June 2006

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Can It Get Even Better Than This? Continued

Where do you go from here?

Start by getting in touch with the way you eat and live.

The news from HIV research and care centers is that being on HAART increases the risk of heart disease. Fat carried in the gut area contributes to elevated cholesterol and insulin resistance, a contributor to diabetes. High blood fat is part of it; irritations from medicines play a part, too. Lifestyle stuff—excess weight, cigarette smoking, lack of exercise—also contributes.

Step back and take a look at how well you are really eating these days. Maybe write down everything you eat for 3 days, including one weekend day, and size it up against the checklist here. The goal is to get as close to this list as possible so your body works as well as possible and you feel good...or even better.

In making changes in your lifestyle, discover the benefit of some extra focus on diet and nutritional supplements. There are small steps, like my dinner companions and I sharing one dessert as a step toward weight management, and bigger ones, like trying a protein-fruit-nut breakfast for a few weeks. Explore what high quality vitamins or other supplements might do for your energy levels.

The bottom line is that there are many steps you can take to help control the effects of HIV disease, antiretrovirals, and aging. The important thing is to start.

References available at www.tpan.com.

Charlie Smigelski is a Registered Dietitian who has been with Fenway Community Health Center, one of Boston's primary HIV treatment and research centers, for 14 years. His special emphasis is on how diet and supplements can reduce or reverse side effects of HIV and HAART, and helping people live more comfortably with their medical regimens. He is the author of Eat Up! Nutrition Advice and Food Ideas For People With HIV and AIDS. Positively Aware, Fall 2006 Special Issue

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**I keep six honest
serving men (they
taught me all I knew):
Their names are What
and Why and When
and How and Where
and Who.**

Rudyard Kipling

