Blood from a Stone

People with HIV and hemophilia will be ignored no more

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You can hear Pat Buchanan saying it: Promiscuity leads to AIDS. Well, how would you like to be forced to have unsafe sex with up to 60,000 people in an instant? This is Jonathan Wadleigh's take on what it's like every time he injects himself with a clotting serum that will keep him from bleeding excessively. Wadleigh has hemophilia. He's also positive for HIV and hepatitis C because blood-products companies decided that pooling the blood of thousands of people to create this serum -- without proper screening -- was an acceptable risk that people with hemophilia would have to live with. Of course, it also happened to satisfy the manufacturers' bottom line.

This "promiscuity" is nothing new to the hemophilia population, whose members are routinely exposed to numerous pathogens. In fact, medical professionals realized as long ago as World War II that hepatitis was being transmitted through the blood supply. Blood banks ignored the risks. Now, 50 years later, things have gotten progressively worse. Ninety percent of people with severe hemophilia were infected with HIV between 1981 and 1984. Ninety-five percent of them are also hep C-positive, and more than 99 percent have hepatitis B or have been exposed to hepatitis B at some point in their lives. And it doesn't stop there. Many other strains of hepatitis are swimming around in the blood supply, and a blood donor recently died from Creutzfeldt-Jacob (mad cow) disease. (The company put a recall on the batch that donor's blood was pooled into, but only months after it was distributed.) While the American Red Cross issued a statement earlier this year insisting the blood supply is safer than it has ever been, the hemophilia community is not satisfied. "What does that mean?" asks Wadleigh. "Is it less horribly contaminated, or is it truly safe?"

New genetically engineered forms of clotting factor have been developed that can reduce the risk for those who can afford them. But they cost two and-a-half times as much. For people who can't afford them, intermediate-purity factors exist that continue to spread pathogens throughout the hemophilia community.

What we're left with is a community of guinea pigs that has come to expect new viral infections like others expect the common cold. Val Bias, a lobbyist for the National Hemophilia Foundation (NHF) in Washington, D.C., tells of his own experience as a child whose doctor wanted him to get hepatitis at a young age -- the implication being that sooner would be better than later. Now Bias, 38, asks the question of legislators on Capitol Hill: If you had to go in for a preplanned surgical procedure, would you use the hospital's blood -- or donate your own in advance?

At age 50, Wadleigh's ankles are so badly arthritic that he needs to walk with crutches. The use of crutches, in turn, causes shoulder trauma and hemorrhaging into his elbows. He also has artificial knees. Until clotting factors were released on the market in the late '60s, hemophilia had been very difficult to treat. The condition is characterized by the body's inability to produce proteins, factor VIII and/or factor IX, that aid in blood clotting. The result is hemarthroses or episodes of joint bleeding, spontaneous or trauma-induced. Hemarthroses can severely damage joints and cause hemophilia-related arthritis. Those born after the antihemophilic clotting factors were introduced were often spared the debilitating joint problems.

"I'm one of those people who's been through the whole gamut of products that were used to try to alleviate the bleeding," says Ron Niederman, 46, a board member of the Hemophilia Association of New Jersey. "I took everything from whole blood to frozen fresh plasma." But it didn't do him much good. Both Niederman and Wadleigh had rough childhoods because of the joint damage, and later ended up with HIV as well.

Add the exacerbating effects of HIV and its concomitant treatments to the problems of bleeding and hepatitis-related liver dysfunction, and you have a set of considerations that must be kept in mind when treating these conditions. They are serious concerns to most people with hemophilia and their providers, but opinions differ on exactly how strong the concern should be.

Corey Dubin, president of the Committee of Ten Thousand (COTT), a group organized to advocate for the 10,000 hemophiliacs infected with HIV in the early '80s, believes that antiretrovirals are often too toxic, especially to people with hemophilia. "I've seen too many friends die of AZT poisoning," says Dubin, "and I don't think we should be getting less critical of drugs that are in the queue for approval." Dubin has even asked the Food and Drug Administration (FDA) to create a standard of care for people with HIV and hemophilia.

But Stephen Hauptman, M.D., who has a hemophilia/HIV practice in Philadelphia, feels strongly to the contrary. "I don't see any drug as a particular problem among hemophiliacs," Hauptman says. "Patients have been much sensitized to go to hemophilia docs who are keyed into liver enzymes, but I think it's an insignificant issue." He acknowledges that protease inhibitors are suspected of raising liver-enzyme levels, but his experience with Crixivan, the Merck & Co. protease inhibitor, is that it has no effect on the liver enzymes of people who already have mild to moderate elevations. He has even found people with hepatitis and systemic Mycobacterium avium complex (MAC) -- which settles in the liver -- to have benefited from Crixivan.

Rich Colvin, internist and COTT board member, sits somewhere between Dubin and Hauptman. Two of Colvin's best friends died of liver failure -- not necessarily an AIDS-related illness -- so he is reluctant to call the risks or side effects insignificant. "[Closely monitoring liver values] is worth considering when the liver is having trouble," Colvin says, "especially because the liver metabolizes a lot of HIV medications. It also remains unclear what the natural course of hep C infection is, so it's important to keep an eye on it."

In addition to monitoring traditional markers of HIV progression, he explains, one should always

monitor liver function as a baseline. Know the hep C antibody status. If it's active, look at the hep C viral load using the same PCR test that is used with HIV. Treating the liver or changing meds, however, should be delayed until enzyme levels are persistently elevated. At the moment, the only treatment for hep C is alpha-interferon, but data are inconclusive on how well that works.

Robert Keller, M.D., supports monitoring, but feels that people with hemophilia tolerate HIV meds just as well or as poorly as nonhemophiliacs. "You have to be more careful in the hemophiliac population regarding the meds that may affect liver function," says Keller, "but that's certainly no reason not to put them on appropriate antiretroviral therapy." Keller avoids ddI and ddC to stay on the safe side, but for the most part, he has found no major problems in people with hemophilia. Niederman, for example, took part in Protocol 193A, a study of AZT, ddI, ddC and 3TC in combination. His liver enzymes went through the roof, so they had to reduce him to half-doses in order to complete the trial. Before that, he was taken off the MAC prophylaxis rifabutin for the same reason. But Niederman says these are not uncommon reactions in the general HIV population.

A self-proclaimed "born and bred" immunologist, Keller approaches his HIV/hepatitis/hemophilia work with an attractive obsession with immune-based therapies. At Biodoron, his Florida HIV clinic, he not only attacks the subject with enthusiasm and optimism, but he is also conducting a statewide protocol of a natural alpha-interferon called Alpha Leukoferon, made by the Florida-based biotech Viragen. This new compound is said to contain most, if not all, of the 25 subtypes of alpha interferon the body manufactures. "Alpha-interferon is probably one of the most potent antiviral substances in the body," Keller says. "If you pick one subtype only, as the manufacturers of Intron or Roferon did, then you are optimizing for function of that subtype and neglecting the functions of all other subtypes." And because people with hemophilia turn up positive for most strains of hepatitis, he explains, it is important to cover as many subtypes of alpha-interferon as possible.

In his quest for the quintessential immunological balance, Keller has also discovered that both bleeding and the administration of clotting factor up-regulate (or kick-start) the immune system. "An up-regulated immune system is an easier target for HIV. If your immune system is never activated, HIV can never reproduce," Keller says. He has found that by administering a timed weekly dose of factor to coincide with those days when patients are most likely to do damage to themselves -- he asks patients to keep an activity log -- they can reduce the need for factor and reduce the number of bleeding episodes by at least 35 percent.

Colvin also finds special cases of bleeding where the caregiver and patient need to take extra precautions. With liver disease, for example, a biopsy may be desired to assess liver damage, but for a person with hemophilia, this requires an invasive procedure, which may induce bleeding, so prophylactic clotting factor is necessary. This also holds true for drawing blood from an artery to obtain blood-gas readings, for example, and for spinal taps if the presence of cryptococcal meningitis must be determined. In the case of people with hemophilia with thrombocytopenia -- a blood disorder characterized by low platelet count and cranial hemorrhaging -- steroids are often used to keep the body from rejecting platelet administration. But for people with HIV, the

immunosuppressive action of the steroids should be avoided. In that case, Colvin believes that prophylactic clotting factor three times per week can partially make up for the low platelet count.

For Ron Niederman, who had an eight-week bout of kidney stones caused by the sulfates in Crixivan, bleeding was a painful ordeal. His particular case of hematuria, or the presence of blood in the urine, would only resolve itself with factor VIII treatment and 14 glasses of water a day to prevent the formation of more stones. In addition to this relatively common Crixivan side effect, this past August 15, people in Europe who had been taking protease inhibitors reported spontaneous bleeding. The FDA response was a simple statement of caution that health care providers monitor their hemophilia patients more closely.

Charla Andrews, director of research at NHF, is irritated by the lip service given by FDA and drug companies alike when red flags like this go up. She thinks if the clinical trials were thorough to begin with and had the proper representation of people with hemophilia, such risks would be known in advance. “If only 12 out of 1,500 people in the trial were hemophiliac, and one out of every 100 hemophiliacs have abnormal bleeding, then the study may never discover this side effect,” explains Andrews.

In 1987, the NHF AIDS Clinical Trial Unit (ACTU) was conceived to specifically address the exclusion of the hemophiliac population in HIV drug trials. Starting early on, AIDS clinical trials have had restrictive entry criteria, especially about markers of liver function. Andrews has even found this to be the case more recently with the protease-inhibitor trials. Coagulation studies, done as markers of toxicity, were also very difficult for people with hemophilia to break into, due to concerns among drug companies. “There was a level of discomfort from infectious-disease docs dealing with what they considered fragile patients,” Andrews says. “If there was one slot open in a trial and two people wanted in, they would choose the person without hemophilia.”

And HIV negative people with hemophilia take precedence over PWAs in hemophilia-specific drug trials, such as the new bleeding-disorder treatments currently in development. “We’re sent to the back of the line,” Bias says. “A new synthetic blood product is now being tested, and they’ve set the T-cell count at 350 or above. That keeps a lot of us with HIV out of the trial.”

The general consensus on most fronts is that combination therapy with protease inhibitors is the most promising treatment regimen yet. But people like Dubin are not always optimistic that people with hemophilia and HIV are getting the best HIV care at the federally funded hemophilia treatment centers (HTCs). “The consistent complaint is that the HTCs have not brought on board people who are on the cutting edge of HIV treatment,” Dubin says, “because the providers have treated the hemophiliac since birth; there is a level of paternalism, that is, the person should not question the doctor’s judgment.”

Megan Schirle, a social worker with the Alta Bates Medical Center, an HTC in Berkeley, California, agrees, although Alta Bates does not fit the profile of most HTCs. The director, an infectious-disease doctor, was hired in 1983 to head the adult treatment center. “HIV was another layer of secrecy and trauma,” Schirle says. “The impact of having several family members infected with

HIV was overwhelming. Even treatment center professionals were blown out of the water.” She believes a lot of mistakes were made in regard to how testing was done and how to handle disclosure.

Today, primarily because of the HIV epidemic, people with hemophilia are a lot less timid about demanding good health care. At press time, Bias was lobbying for a billion-dollar bill called the Ricky Ray Hemophilia Relief Fund Act, which would give each hemophiliac infected with HIV compensation of $125,000. (This is separate from a lawsuit against blood-products companies.) But money isn’t the issue that stirs up people like Bias. “If HIV had been the only infectious disease the hemophilia community had to deal with, I don’t think we would have this bill,” Bias says. “But when you’ve been exposed to numerous viruses and lost entire families, you begin to ask: How long do individuals have to be on the front line of the blood supply and get nothing in exchange?”
