The Road to Wellville

If Sean had followed the advice of many experts, he might not be here today.

May 1, 1999 By Lark Lands, PhD

For five years, POZ *founder Sean Strub has bared his labs to the world via this column. Readers have had a front-row seat for the wild swings of his health, reflected in medical test results and analyses by every kind of medical expert. This month, pioneering AIDS clinician and researcher Joseph Sonnabend, MD, reflects on his patient's roller-coaster ride—and the lessons it might offer for the many other PWAs who've been riding with him.*

In 1994, when Sean founded *POZ* and first came to me, he was in great danger of dying. Both his CD4s and his white blood count were extremely low. He was having fevers and nightsweats. He had recurrent diarrhea. He was fatigued. He was anemic. He had lost 10 percent of his normal body weight. He was, in sum, a very sick guy.

In those days, symptoms like Sean's were often not worked up using every available diagnostic tool. All too often they were just looked at as an inevitable consequence of the disease, an attitude that I thought was stupid and defeatist. Frequently, treatable causes could be found if you tried hard enough.

In Sean's case, my efforts to pin down the cause of his fevers were unsuccessful. But I did start him on prophylactic medications (clarithromycin for MAC and Bactrim for PCP). I also put him on the drug Neupogen to restore his dangerously depleted white blood count. In addition, I had him eliminate dairy products—a frequent cause of diarrhea due to lactose intolerance. The results of these changes were dramatic: His diarrhea was eliminated, his weight began to return, his energy improved and the fevers disappeared. It is unclear which step played the most important role, but it's possible that the prophylactics—which are broad-spectrum antibiotics—happened to treat an infection I was unable to diagnose.

In many ways, the difference between life and death back then was good doctoring: how quickly you diagnosed an infection and how effectively you treated it. Since most people were dying of things at least partially treatable, good doctoring could go a long way toward keeping people around. I thought that was far more important than jumping to try the first antiretroviral, and Sean agreed.

It now seems very important that Sean did not join the AZT monotherapy bandwagon. I believe

that his skepticism about this drug may be one of the reasons he's alive today. As a clinical researcher, I had reviewed data on the first AZT trial, and it seemed likely to me that factors other than the drug may well have contributed to the striking survival difference between those on AZT and those on placebo. And as a virologist, I felt that using this type of drug in high doses over the long term was highly questionable and was quite likely to cause serious side effects.

Sean's decision to delay therapy was controversial at the time. Even today, many are being pushed to start therapy very early despite our lack of knowledge about when it's optimal to begin. We urgently need controlled clinical studies to assess this, not just the opinions of "experts" sitting on panels. If Sean had followed the advice of many "experts" early on, he might not be here today.

Sean had very high viral loads in those years (from 1 to 3 million) and very low CD4s (ranging from one to seven). In the summer of 1994, he developed external Kaposi's sarcoma (KS). By November 1995 it had spread to his lungs—a condition that at the time was almost always fatal. Luckily, the then-experimental chemotherapy Daunoxome helped, with the skin lesions fading and the lung ones stabilizing but not disappearing.

Because the research on ddI appeared to show some survival benefit, Sean began it in October 1995, with a resulting big drop in viral load. Unfortunately, after a few months he developed pancreatitis and had to discontinue it. In March 1996, he began his first protease inhibitor, ritonavir (Norvir), along with 3TC (Epivir). His viral load dropped from 700,000 to 70,000 and his pulmonary KS began to recede, but the combined side effects of the KS chemo and ritonavir caused severe nausea, vomiting, and diarrhea. So in July 1996 he switched to indinavir (Crixivan) with d4T (Zerit), and in August added delavirdine (Rescriptor).

I would call this combo the real breakthrough for Sean's health. His viral load became undetectable; his CD4s began to climb significantly; his blood counts improved; and he felt remarkably better, with much of his old energy restored. And in perhaps the best indication of some immune function restoration, after a number of months on this antiretroviral trio, his KS completely disappeared from his lungs. There is no doubt that HAART saved Sean's life.

Alas, it has come with complications, including lipodystrophy-associated wasting in his limbs. Although this was successfully treated with human growth hormone (Serostim), I am concerned about Sean's long-term risk of heart disease, especially because his lipid (cholesterol and triglyceride) levels have been quite elevated for at least a year. I think it's terribly important for Sean and all others on HAART to test blood pressure regularly, and look at all risk factors for heart disease: family history, diet, smoking and exercise habits. Doing regular lipid profiles should be standard. And all risk factors should be addressed to the greatest extent possible: Stop smoking (Sean never has), start exercising (unfortunately, he's rarely done that either), eat a good diet (he's improving). If blood pressure is elevated, try to reduce it with diet, exercise and meds, if necessary. For those on testosterone or other anabolic steroids, regularly monitor hematocrit, which if elevated indicates a possibly increased risk of heart attack.

Of course, Sean doesn't always follow my advice on this or many other things. But there may be

lessons from his experiences when he ignored me. A case in point is his unplanned two-week drug holiday last summer. His skyrocketing viral load (peaking at over a million), crashing CD4s (down from 357 to 154) and immediate return of symptoms obviously motivated him to continue the meds as directed. It is encouraging that when he restarted the drugs, his viral load dropped to 501 within three months. Today that reading (listed on his lab report as **HIV-1 RNA ULTRAQUANT**) stands at 299, with his CD4 count back up to 383. This may offer some support for the idea that total holidays—stopping all drugs completely for a period of time—could allow someone to successfully return to a previous regimen. However, until controlled trials of temporary drug cessations clarify the possibilities for boosting the immune response in this way, I certainly wouldn't advise it, especially in someone with advanced disease. But the riskiest thing is taking drugs erratically. I would tell anyone that it's terribly important not to stop your drugs, but if you're going to, then stop everything. Do not remain on a suboptimal regimen. If Sean had dropped to two drugs, he might not have been able to use those drugs successfully again.

And that would be a disaster. Sean was brought back from the brink of death by HAART. I hope his restored health will last, although with the tendency of drug-resistant strains to develop, the benefits of any regimen will most likely wane eventually. This makes it urgent for scientists to move quickly on developing new classes of antiretrovirals and new approaches to immune restoration. Even with these caveats, I do think that Sean's story should be an encouragement to others.

JUNE 1994
"Sean's CD4 count (107) stands out. If it falls much more, he'll be at risk for severe infections. There will be toxicity from AZT and other drugs. Treat with meds that have very low toxicity."
—Susan Diamond, MD

AUGUST 1995
"Sean's viral load is high at 3.3 million copies [and his CD4 count is 6]. This picture is one of high-level viral replication that's going unchecked. I would guess that Sean's risk of an OI within the next year is high. Sean could achieve a lower viral burden by beginning antiretroviral therapy."
—Michael Saag, MD

MAY 1996
"It's hard for me to say this, but I think Sean's a little worse than he's been. He has extensive KS on his face and in his lungs. He's fatigued and has problems with his moods. I think he's holding on, but he's a very sick person."
—Joseph Sonnabend, MD

MARCH 1997
"Sean must be quite elated. After months of combination therapy with a protease inhibitor, his CD4 count has risen markedly, to 77, and his HIV viral load is indetectable. More important, he feels well with increased energy and improved KS. Can he jettison the preventive therapies taken to avoid opportunistic infections? We don't precisely know yet."

—Donald Abrams, MD

OCTOBER 1998

“After almost two years with an undetectable viral load, Sean initiated an unplanned drug holiday for two weeks. Within 10 days his viral load skyrocketed. He also experienced severe fatigue, swollen lymph glands, headaches and a malaise that left him unable to work. This occurs when one’s system is overwhelmed by an influx of virus.”

—Virginia Cafaro, MD

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