

An interview with Stephen H. Schneider, PhD, Department of Biological Sciences, Stanford University

## The patient from hell

By Randi Londer Gould

**S**tephen Schneider was diagnosed in 2001 with rare and deadly mantle cell lymphoma. An internationally recognized expert in global warming, Dr. Schneider approached his cancer treatment using the same skills in decision analysis that he employs in his research on climate. Certainly he is not a typical patient. A member of the National Academy of Sciences and a 1992 recipient of a MacArthur Fellowship, the so-called genius award, Dr. Schneider—along with his chief advocate, his wife Terry Root, PhD, a Stanford biologist—was able to summon the intellectual and financial resources needed to fight his disease. He wrote a book about his care (*The Patient From Hell: How I Worked with My Doctors to Get the Best of Modern Medicine and How You Can Too*, reviewed in our November/December 2005 issue), in the hope that doctors and cancer patients alike would benefit from his experience in assessing risk and making decisions in the face of few data. We spoke with Dr. Schneider at his home in Stanford, California.

**Community Oncology: If you wanted to design an ironic situation, it couldn't be more poignant than this.**

At the time of my diagnosis there weren't that many mantle cell patients, and there was no well-developed protocol. Doctors had to wing it. I said to my physicians, "So the gods of irony have given me a research disease for which there's very few data? Do you have operating experience? Do you have knowledge of process?" They agreed that that's what we would have to use.

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**What were some of the most important parallels between your work as a climatologist and your new "job" as research scientist on your own disease?**

In climatology we use the best in physical, biological, and social sciences to construct models. That empirical knowledge is clinical trial-like. The trouble is, when you go far out into the future, you're in "no-person's land" because now you can't be sure whether the assumptions that went into constructing those climate models will still be true. We can test and validate models against events in the atmosphere like a volcano blowing up, throwing dust in the stratosphere, and cooling the temperature. This is not a perfect test of global warming, but it's the kind of surrogate experiment you conduct to understand the processes that make the model work, and to make sure it's operating consistently. The more consistent it is, the higher your confidence. So you use scientific judgment, and in fact, that's how we make climate predictions. I wanted to apply exactly the same kind of principles in treating my disease, because there weren't any significant clinical trial data for mantle cell lymphoma. Yet there were a lot of anecdotal reports and small studies in the literature—more than enough, I thought, to formulate opinions about best-of-the-moment treatments.

**You've managed to rile up some oncologists by saying they're stuck in an evidence-based medicine rut.**

I'm not against clinical trials. I want the data, but what do you do when you don't have any? Most of us with dread diseases and not much

to go on are willing to do some experimentation. If we can help doctors learn more quickly, even without a formal clinical trial that would take years to yield results, I think we're doing something of value for ourselves and for other people.

**Your grand experiment was wanting to use rituximab [Rituxan] for maintenance therapy. But the gods of irony had to intervene again for that to happen. Tell us about it.**

After going through R-CHOP chemotherapy, whole-body radiation, and an autologous bone marrow transplant, I wanted to make sure we kept



Stephen H. Schneider, PhD

residual cancer cells at a minimum; in fact I wanted a hard zero. I convinced my docs to use PCR [polymerase chain reaction] monitoring to keep an eye on residual disease. I knew that a second remission is much harder to achieve than the first, and if we waited for tumors to show up on a CT scan it might have been too late to use low-

dose or low-impact interventions. I thought it made sense to use Rituxan for maintenance therapy. But I had to fight for 2 years to get it.

My doctors thought it was a good idea. But we disagreed on when it should be administered. They wanted to wait until PCR showed 3 successive results of cancer cell increases; the numbers were bouncing around from 78 to 49 to 101 and then to 20 and

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so on. They thought there was some small risk of the Rituxan causing immunosuppression. But I was willing to take the low risk of using the drug in order to avoid the high risk of the cancer count building up and being hard to reverse. So we went back and forth.

In December 2003, my wife Terry and I were in Italy for a conference. Afterward we visited Dr. Alessandro Gianni in Milan, a leading researcher in PCR and Rituxan for mantle cell. I wanted to find out about his protocol. He conceded that no one knew what concentration of cancer cells in a PCR test separated a dangerous level from background noise. But he also questioned why anyone would take the risk of not treating probable residual cells with Rituxan. He said to us, “Why don’t you just make the assumption that there’s too high a probability the cancer has come back, and you should treat it as a precautionary measure?” That is exactly what I argue in climate all the time. We don’t have to know that we will have the worst outcome in order to act. At first I couldn’t convince my doctors, so we were at a stalemate.

Then I came down with severe edema—at one point I had 10 or 15 pounds of extra fluid in my legs. It was traced to a rare kidney disease called membranous glomerulonephritis [MG]. At the time, a just-published paper

suggested that Rituxan could effectively treat MG. Out of eight patients with the disease, all of whom were given four Rituxan treatments over the course of a month, seven showed substantial improvement after a year. So my kidneys did me a favor by getting the doctors to give me Rituxan, which I now take once every 3 months for mantle cell maintenance. There are about a dozen of us in the United States, along with a few patients in Europe, who are the calibration points for PCR and Rituxan maintenance treatment for mantle cell. We should know soon how effective it is. So far, so good!

**In your book you talk a lot about weighing economic costs and benefits. Was this a concept that met with resistance during your initial treatment?**

I had to “earn” Neupogen after my chemotherapy; at the time it was the hospital’s policy. The hospital’s primary concern was their private costs. I teach cost-benefit analysis and good economists know that economic efficiency is the sum of private and social costs. The social cost to Stanford and to society of my missing a week of work is in the thousands of dollars. That’s a lot compared to how much the drug cost, which may have been on the order of \$500 to \$1,000. So to save themselves a little money, they put me at risk, which resulted in high social costs. I felt we needed some legislation about this. That’s why I decided to write the book.

**But don’t doctors have to be cost conscious, especially in this new age of reimbursement cuts?**

I think my doctors at Stanford were frustrated by the policy, but they couldn’t fight City Hall—in this case, the hospital and their accountants.

**So how easy is it going to be for the practice-based oncologist to make the kinds of shifts you’re talking about when he**

**or she is fighting insurance companies and Medicare?**

I’ll give you another climate analogy. There was a famous bumper sticker back in the 1970s, that said you should “think globally and act locally.” In other words, if you think about global warming, you should control your tailpipe emissions at home. But there were no incentives to do that because there were no emission rules. I think the bumper sticker got it backwards: you have to think locally—that is, ask how we can have the incentives to get things done—and then act globally so that everybody is in the same boat following the same mandated standards. In other words, the recognition of social as well as private costs has to be built into the system so that a particular practice isn’t punished with inadequate reimbursement when they give good care. I don’t see how that’s going to change without acting globally, which in this case means changing policy through national legislation.

**Your own experience has shown that cost effectiveness and quality care can go hand in hand.**

Absolutely. I argued strenuously to get PCR, and that test is expensive. But it can uncover minimum residual disease. That then leads to treatment which prevents the patient from getting full-blown cancer and needing high-dose chemotherapy, and another bone marrow transplant, which not only poses risks but costs the insurance company some \$300,000. Suppose we could stall that by just 1 year with an individualized PCR test that costs, say, \$5,000. That’s a good return on investment.

We’re looking for the win-win when a treatment is both cost beneficial—that is, the sum of private and social costs—and at the same time cost effective from the perspective of the healthcare provider. I would argue that it’s in the hospitals’ and the HMOs’ interest to stall a bone marrow transplant 1 year. Supposing they

can stall the bone marrow transplant 2 years? Now, they're really winners. Supposing they can prevent it altogether with a maintenance package? Maintenance costs money, but is it more or less than the bone marrow transplant? Probably less, although some designer drugs are very expensive, so you have to look at individual cases. But that's my point. In climate as in medicine, we have to do whole-systems analysis.

**You and Terry have the intellectual and financial resources that a lot of people don't. If most patients can't muster that, how is your book going to help them?**

*The Patient From Hell* is aimed at two audiences. One audience is doctors, because I'm an outsider, and I don't know the ins and outs of all the details. I only have my experience, my knowledge. It's up to doctors to decide how they want to fix their own establishment. But I can push a little bit and point out some parallels to decision analysis.

My other audience is patients. I've had more than 100 people write desperate e-mails to me about their mantle cell or other cancer. It has been heart-wrenching. They want my advice, and I always say the same thing: "I'm not a doctor; I'm not competent to give you advice. But I can tell you the questions to raise with your doctor so that in your specific case you can work out what makes sense." And if people don't feel up to it, I suggest that maybe they have a relative, a family doctor, or a retired doc in the neighborhood who'd be willing to be their advocate, someone who can intercede, do research on the Web. Terry would routinely give a fistful of downloads to my oncologist who would read them. My doctor changed things in my treatment, because she thought about it and discussed it with her colleagues. So the doctor with a good ego is the one who's not threatened by this.

**Luck played a role in your treatment. Just before your first biopsy you went with Terry when she happened to have an appointment with her breast surgeon. Her doctor suggested you have an extra lymph node taken out and frozen for later PCR study.**

When I mentioned this to the senior surgeon he said, "Hey, that's a good idea," and he did it happily. This is the kind of stuff that I don't blame anybody for not thinking of. If we can help doctors by searching the Web, and keeping up with things, and they have an open mind, then I think patients can actually be partners in their own treatment.

**In the book you talk about mourning your illness. Is that a process you're still going through?**

Oh, yeah. After my bone marrow transplant when my white counts were returning and my immune system was on its way back toward self-sufficiency, I just cried. I didn't know what was going on, I couldn't figure it out. So I called a psychiatrist friend, and he said, "Let's see: For the past 6 months, you've been running your own show, you've been your own advocate, you haven't had time to feel what you have. Aren't you angry that you had cancer? Didn't you ever say, 'How the hell did this happen to me?' and, 'What'd I do to deserve this?'" I'd had all those thoughts but I had just banished them. The psychiatrist pointed out that I had been so focused on just marching up the hill to come up with what I thought was the best treatment. Now there was nothing more for me to do. He said, "There are no further decision points. Just let it flow over you. Feel all your pain and anger and hurt and fragility." And he was right. I did that. The emotions come back now when I get e-mails from people whose spouses have mantle cell, and they're trying to deal with doctors who are not quite up on the state-of-the-art.

**In fact, a recent survey of community oncologists showed there are some significant barriers to staying current.**

Maybe there need to be rewards for going to medical meetings. You have to set up incentives. If there's a disincentive for you to be out of the office for a week—and not just in terms of lost income or the costs of the meeting, but in terms of the patients who need you because there's nobody to back you up—the system is perverse. It's actually giving people incentives to stay stuck in traditional protocols without the opportunity to learn faster. So I think the medical community at large has to take some responsibility for the "main-

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tenance therapy," if you will, of keeping people up to speed. The more integration across people's different skills, the better it will be for patient care, and in the long run, the better it will be in terms of keeping costs lower.

**This is a tough problem for community practitioners who are so busy taking care of more than 80% of this country's cancer patients.**

A well-known national medical figure—I don't want to mention names—said to me in a challenge, "Steve, what are you going to do"—and please don't be offended in Broken Bow, Nebraska—"when a two-person community oncology practice in Broken Bow, Nebraska, that treats every cancer patient for 200 miles around is so busy they can't go to oncology meetings, they're not up-to-date on the latest Web stuff. Do you want them to make protocol exceptions?" And I said, "No, I don't. But why can't Stanford, and Sloan-Kettering, and Hopkins, and all the

places that have fellows—why can't they come up with individualized tests to find out whether a person is more or less likely to benefit from certain kinds of drugs? Why can't they come up with a subjective probabilistic assessment that shows when it doesn't work so you can change gears and put on the Web what these tests are." You can have protocols A, B, and C that can be linked to individualized tests. It would be a way to try to get a compromise that makes treatment better than what we have now and doesn't ask the impossible of people who are delivering the necessary service.

### **So you don't think treatment guidelines are adequate.**

I'd like to see the guidelines refined so that they're more individualized. And that doesn't mean that the doc out there, who's not a front-ranked researcher, is supposed to figure out how to individualize them. I think that the research community can give guidance on that. Since community oncologists are recruiting 60% of the patients who are in clinical trials, I think they can feed back information they are getting on the local level, to the academic researchers.

I'll give you a metaphor I used with my cancer team that made them laugh and helped me get individualized PCR. I said, "Supposing the Martians are the solar system's best cancer docs; they're light years ahead of us, they take pity on us, and they come down, and say, 'You don't need to do clinical trials, we're going to give you the answer.' They're going to tell us the average remission length for each of 300 cancers, and for each of 1,000 drugs. So, I asked my doctors, "What would you do with that information?" And they said, "Well, of course, we're going to give the drug that has the best results." And I said, "The best results for whom?" They said, "The patients," and I asked, "Which patient?" "The median patient."

But what if your patient is far away

from the median, and she doesn't need a full-blown dose? You're overdressing her. What if she's far away from the median on the other side, and she needs more? Can't we try to individually tailor diagnostics? Because even if somebody gives us the median answer, it's not enough. They're not telling us where an individual sits in the bell curve. So, we need to refine. We don't have to fill in every single blank, but maybe we can have a category of less, more, and in the middle—something that's better than just assuming everybody is that mythical median.

### **There is one thing you can pretty much say about all cancer patients: they feel incredibly anxious when they have to wait for test results. Did you see any movement on the part of your hospital to speed up that process?**

Not at first. The agony was the PCR tests. Sometimes the results took weeks. I tried to put it out of my mind, but it was always there: that gorilla, the one I thought I had knocked down, stirring in the background. Over time, I think they realized we could be trusted not to misinterpret the information. One of the fellows knew it was okay to violate the prime directive, which is, "Only the doctor gives test results to the patient." This fellow wasn't the primary doctor, but she had approval to e-mail the results as soon as she got them. They were mostly good. But when the counts were up, it gave Terry and me time to do more research on the Web, think about what we wanted to discuss at the next visit to focus our conversation and save all of us time.

### **In spite of your anxiety, could you see things from your medical team's point of view?**

I don't know how oncologists can take it. This is why I got into climate where you can "save the world" from the pulpit and you don't have to see the misery of the individuals who've been flooded out by the sea level rise.

You can look at it academically. As a left-brained person, I was comfortable looking at efficacy of cancer treatments and their cost effectiveness. But if I had to actually sit there and meet frightened patients, that would be hard. I really admire these docs and nurses for doing it.

### **By the way, do I detect even a whiff of apology in your book title—*The Patient From Hell*?**

Yes, it's more than a whiff. We were a pain in the ass!

### **But do you need to apologize for that? It's your health.**

If I thought the doctors were willful, lazy, or money-grubbing, not only would I not apologize, I'd aggressively go after them. But they are none of those things. They're just very busy, constrained by insurance issues, and not heavily trained in decision analysis, which should be taught in medical school—and not in just a quick and dirty way that doesn't stick because it isn't practiced and isn't taught in depth. It would also help if hospitals had consultants to see them through the tough cases by running probabilities. It's called a "regret matrix" and a lot of businesses use that tool.

### **Is that one of the ultimate goals of your book?**

I certainly don't think the book is going to solve all the problems. I don't have enough perspective. I make no claims on special knowledge of cancer, though I've learned a lot about my own disease and my life. When I was going through the transplant, I got a lot of cards and letters and e-mails from people telling me how important I was to them and to their career choices. I said to Terry, "You know, if I don't get out of here, at least my life wasn't a waste of time." That was the silver lining inside of cancer: I felt like I was at my own funeral and I walked out.

*Dr. Schneider can be reached at sbs@stanford.edu.*