Murphy’s Law Breaker

Shots in the Dark, an AIDS-vaccine saga, has it all: mysteries and scandals, best intentions and worst-case scenarios. Walter Armstrong talks to Jon Cohen about his 10-year investigation.

April 1, 2001 By Walter Armstrong

Jon Cohen’s *Shots in the Dark: The Wayward Search for an AIDS Vaccine* (Penguin) belongs next to Randy Shilts’ *And the Band Played On* on your AIDS shelf. Covering two needy, greedy decades and a cast of hundreds, Cohen’s muckracker combines the suspense of a thriller with a rare moral urgency to remind us of how institutional inertia and individual indifference allowed this epidemic to happen. But Cohen, a staff writer at *Science* and *Talk*, work-at-home dad and San Diego surfer, goes one better than Shilts by offering a blueprint for reform.

POZ: *Wayward Search* doesn’t even begin to cover the story you tell, in which everything that could go wrong seemed to.

Jon Cohen: The biggest problem has been scientific: HIV is a tough bug to beat. In the book, I describe the virus as an arsonist that targets firehouses -- it attacks the very immune system that exists to defeat it. If HIV were, say, poliovirus -- which can simply be defeated by antibodies -- we’d have a vaccine. That said, I think the AIDS-vaccine enterprise has allowed many promising leads to languish, shunned coordination, been seduced by technology and faddishness and had trouble applying basic-research insights.

Part of the problem is the culture of American science and the National Institutes of Health [NIH], which are great at advancing knowledge and fueling creativity, but aren’t set up to make products as quickly as possible. And the system works pretty well when industry and activists get involved -- there are now 15 antiretrovirals on the market and many more in the pipeline. But big pharmaceutical companies have shown little interest in developing AIDS vaccines. Many biotechs are making them, but they’re cash-strapped and prone to hype because hype’s all they really have to sell.

What first got you writing the book?

In 1989 I wrote an article for *Science* about the state of the field and was stunned that most researchers were dismissing what seemed to me the most promising approach -- the whole, killed virus. Monkeys can be infected with SIV, a cousin of HIV, and that year a few labs showed for the first time that a vaccine made from killed, whole SIV could protect the animals.

And the personalities also fascinated me. On the one hand, Robert Gallo’s camp was contending

that the best way to make a vaccine was to genetically engineer HIV's surface protein, gp160, or a smaller piece of it, gp120. This idea had little data to back it up, but it made sense mechanistically and appeared perfectly safe. In the other camp, old-timer Jonas Salk was saying, "Who cares about mechanism?" The whole, killed approach worked in monkeys and, he said, could be safely manufactured. I thought, "This is unbelievable: Here is Salk fighting the same battle he did 40 years earlier during the polio-vaccine controversy, with the medical establishment once again saying, 'Don't waste your time with that.'" The situation had an epic, tragic, history-repeating-itself feel.

Which vaccine looks most promising?

I don't know which vaccine is best. Right now there are three dozen in human trials. Only one has made it to a real-world, phase III efficacy test, and few researchers believe that this gp120 vaccine, made by VaxGen, will work. I'm glad to see this trial, as I think the field will progress even if this vaccine fails. We're only going to know whether a vaccine works by staging large three-year tests. The catch is that we cannot test everything. So what should receive priority? As I say in my book, someone, somewhere had better organize an attempt to figure it out.

You offer a blueprint for such an initiative -- The March of Dollars -- modeled on the polio drive, The March of Dimes.

My gut feeling about the AIDS vaccine is, just as with polio, researchers may not have to know everything about HIV to find a working vaccine. A March of Dollars, with public and philanthropic money, could organize this. The main technical problem is the way the research community uses the monkey model. Different labs use different strains of SIV, different species of monkeys, different testing protocols and so on. There is no clear way to compare monkey results from one vaccine to the others. I'd like to see a huge test that creates a public database so that everyone could at least have the same ruler. Then we can say, "Here are the five or six best, safest candidates that work in monkeys. We don't know why they work, but they do work, and that's what matters. So let's put them into humans as quickly as we can with little regard for understanding every last mechanism." It's a radically different way to look at vaccine development, and it's based on urgency.

Maybe my ideas are all wrong. If others have more creative solutions, more power to them. But read my book, and you can't escape hearing that the clock is ticking. And we should remember that a mediocre vaccine introduced today 10 years down the road would save many more lives than a great vaccine introduced five years later.

Isn't the International AIDS Vaccine Initiative (IAVI) up to the task?

IAVI does a good job organizing the effort, prodding the NIH, making collaborations between biotechs and scientists, keeping the issue alive in the world. But much more must be done. IAVI has not staged the type of comparative monkey study that I've outlined. IAVI supports good scientific ideas based on which immune responses are the most important. But that's just one way to approach the problem. Ultimately, of course, it's not up to IAVI. To find a vaccine, we as a society must pull out all the stops.

Many HIVers fear that too much attention to a vaccine will divert resources from treatment.

I've heard that for a long time from activists, who certainly paid little attention to a vaccine until recently, but I don't believe it. I see drug and vaccine research complementing each other. They both build off the same basic research. Companies are always going to favor treatments, anyway, because that's where the big money is.

HIVers also suspect that talk of a therapeutic vaccine may be so much lip service.

As for the therapeutic vaccine, I think it's a very exciting idea, but let's face it, none of the attempts have had anywhere near the dramatic success of antiretroviral therapy. And to a degree, the behavior of MicroGeneSys, which pissed off many researchers and activists by pushing its experimental therapeutic vaccine too aggressively, soured people on the approach.

But a therapeutic vaccine could help, especially if used in people with acute infection who start taking drugs and never have enough HIV in their bodies to properly train their immune systems to mount a robust response [see "LTNP? UB2," page 46]. It also makes sense that in a strategic way, when you stop and start therapy, you could boost the immune system with a vaccine when you are on drugs and not getting the stimulation from the virus. And ultimately I think that therapeutic vaccines will cause less harm than the safest drugs. After all, the immune system is stronger than any antiretroviral.

Your take on the ethics of testing vaccines in humans around the world is that no absolute standard applies.

Ethical problems have dogged the AIDS vaccine since the first human tests in Zaire in 1986. And they've become more complex over the years. One of the most trenchant problems is the success with drugs. If someone becomes infected during a trial and then starts treatment, it's harder to evaluate whether the vaccine works. Maybe the vaccine delayed disease progression, but the drugs mask its effects. Now add into the equation the fact that most poor people still have no access to drugs. Should vaccine testers offer them drugs if they become infected during a trial? Who's going to pay? Is that unduly influencing people to join a trial? On the flip side, some people argue that it's exploitative to stage trials in poor countries unless the sponsors provide drugs. It's a horrible dilemma, and I don't have a simple answer.

Have drug companies intentionally ignored vaccine research because the market of infected people taking drugs for life is more lucrative?

I don't believe the drug companies are doing this intentionally, in a nefarious way. But it's true that the financial incentive to make vaccines is simply not that great as compared to drugs. A vaccine -- you go get your three shots, you're done. That's it, bye. And there are bigger liability issues with vaccines than with drugs. What if your vaccine hurts someone? It's going into a perfectly healthy person. Finally, it's a sketchy market. How many people will buy your vaccine? I document in my book that nobody has a clue. Will gay men line up? College kids? Will parents take their kids to get vaccinated for AIDS along with polio? Will companies be expected to give the

vaccine away for free to the developing world?

Your emphasis on urgency reminds me that people with HIV often say the disease has taught them how to live, because you only have today.

I agree with the philosophy. I want to create a body of work that when I'm on my deathbed, I look back and say I did something that mattered. But I had that feeling before I began covering AIDS. I have my own chronic illness, ulcerative colitis. And my disease is debilitating, too -- not in a life-threatening sense but in day-to-day living a life. When it flares up, I go to the bathroom about 20 or 30 times a day and get incredible stomach pains. I'm supposed to take 16 pills a day, and I have a tremendously difficult time doing that. I have a dream and a will to be healthy, but I also like things that are bad for me like coffee. So I also understand the way that you-only-have-today because even if it makes my stomach churn, well, I'm having my cup of coffee.

Your book seems driven by a moral passion that sometimes verges on despair.

You know, as a reporter covering AIDS around the world, I go in to, say, a South African village where 50, 100 people are dying in a single hospital ward, I take notes, I file my story, and then I come home and I'm just terribly depressed by it. I think that depression -- that sense of vulnerability, of fear, of compassion -- has been entirely missing from the vaccine enterprise. Not from individual scientists, but from the AIDS community. That's why the polio example works so well, because mothers went door to door with pictures of children in iron lungs, on crutches. Each of us must behave as if our own life is on the line. And when that happens, I'll stand down. I'll zip my lips.

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