“The First Cure”

The real drama may be off-stage

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This may be a parable about the vanity and futility of looking where the light is. Also about the virtue of independent thinking and the reward that awaits a true pioneer. Last summer, the Aaron Diamond AIDS Research Center’s first “eradication” candidate was scheduled to stop his therapy. After nearly two years on a triple combo, this twentysomething North Carolinian had no detectable HIV in his body; nor could any virus be cultured from his cells. Dodge, as he was called, was featured on a special *Nightline* segment. “Just one name,” the reporter said, “like Madonna or Prince.” The show was headlined “The First Cure.” But even as the Aaron Diamond team was about to take Dodge off his unpalatable potion to test whether the “cure” had worked, scientists at Johns Hopkins called with disappointing news. After artificially stimulating some of Dodge’s cells in the lab, they made his virus grow anew. If this could happen in a petri dish, they said, it could happen in Dodge’s body. The first cure was not meant to be.

What the *Nightline* program didn’t report was that a similar experiment had already been conducted in France-with much more stunning results. In an ongoing study with the combination of ddI and the 30-year-old cancer chemotherapy hydroxyurea, an Argentinian physician based in Lyons named Dr. Jorge Vila had identified two patients who, after 12 months of treatment, had no detectable HIV in their lymph nodes or blood. The two hale fellows agreed to stop therapy. That was in 1995. Nearly two years later, Vila and his colleagues report no rebound of HIV; nor can they grow virus from test-tube cells.

These results are remarkable: Never before has anyone gone off treatment and kept HIV at bay. In fact, according to current estimates, fully suppressive therapy would have to be given for between three and six years-and possibly for life. The authors propose that hydroxyurea’s success is due to its ability to penetrate viral reservoirs-the “resting” CD4 cells and macrophages that the popular triple combos can’t reach. A drug from the pharmaceutical house that brought us ddI and d4T, hydroxyurea is a neglected child for one simple reason: Bristol-Myers Squibb’s patent on it expired in 1995, so no one’s gonna get rich. (The drug may also cause leukemia and make your hair fall out.) Bristol-Myers recently decided not to finance further research with hydroxyurea.

Although exciting, what all this means remains unclear. It’s inaccurate to say that HIV has been *eradicated* from these two patients: Both still harbor viral DNA. Vila claims that this DNA is defective and incapable of making new virus-a plausible hypothesis. But it’s less likely, at least for

now, that these results can be reproduced in many others. The two men were best-case eradication candidates: Recently infected, treated with no HIV meds prior to ddI/hydroxyurea, extremely low viral loads even before therapy. Other experiments with ddI and hydroxyurea have shown that at most 40 percent of patients go “undetectable.” People with relatively high viral loads almost certainly will not.

Inarguably the Rodney Dangerfield of HIV therapeutics (there’s no money behind it), hydroxyurea is often viewed with impatient disdain by doctors and activists on the triple-drug-cocktail circuit. In fact, the therapy garnered not even a footnote in the recently issued federal treatment guidelines. Rather than targeting HIV directly-as is the vogue in drug development-hydroxyurea inhibits an enzyme inside the body’s own cells, which the virus needs to multiply. And since cellular therapies such as hydroxyurea act on relatively staid human cells-rather than quick-change HIV itself-the emergence of resistance (and drug failure) is much less likely.

Caveats aside, one immutable fact remains: Two HIV-infected people were treated for a year with two drugs (neither a protease inhibitor), went “undetectable,” stopped therapy and almost two years later show no signs of viral reproduction. Is there something unique to hydroxyurea (and other cellular-enzyme inhibitors) responsible for this apparent success? Or will Dodge soon go off treatment and see the same results? *Time*’s “Man of the Year” may be the first to show eradication. Or we may look back on this tiny study of a slighted drug in another country as the true “first cure.” Or perhaps that dream will remain only a titilating title in the land of nighttime TV.

All I know is this: The obvious answer isn’t always the true one; the popular approach is rarely the most effective; and the quick fix, ever so alluring, often doesn’t last. If I were a more brazen risk-taker, I’d bet on a hydroxyurea-like drug. If only because it seems to overcome so perfectly the limitations of current therapies-and it’s a little-noticed drama unfolding off-stage, where the bright light, big money and hubbub are not.

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