Touch That Dial!

A bold new way to treat HIV and trick resistance

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THE DOGMA: To treat the dense resistance many long-term HIVers face, find three or more effective meds. Never start a new combo with fewer than two. If all else fails, try the kitchen sink—a six-plus combo, a.k.a mega-HAART. And always go for undetectable.

THE DOUBTER: New York City's Paul Bellman, MD, and other docs say we need more calibrated strategies to control resistance and make each med last as long as possible. He prescribes "dialing drugs up and down"—boosting them in new ways, subtracting them, even sticking with meds that tests show you're already resistant to—and reducing immune activation(production of the immune cells HIV uses to reproduce) to limit HIV's moving targets. Says Bellman, "Independent of viral load, patients with higher immune activation progress faster, losing CD4 cells too quickly." You may want to tune your doctor into his dogma-defying methods, including:

DIALING UP: Using small doses of Norvir to boost other protease inhibitors (PIs) is a popular and proven tactic: The Norvir monopolizes the liver enzymes that process other PIs, forcing those PIs to linger—and work—longer.Bellman's leap is to play the same game with the nukes, adding low doses of the cancer drug hydroxyurea (HU), whose enzyme-blocking power gives the nukes added oomph. Bellman points out that when the first entry inhibitor, Fuzeon, arrived, some patients quickly developed resistance. Now he adds HU along with Fuzeon, and his HIVers keep on responding.

DIALING DOWN: As opposed to throwing mega-HAART at 'em, Bellman treats some long-term HIVers with dense resistance by subtracting meds. That's because certain mutations apparently reduce immune activation, allowing HIVers to hold on to CD4 cells. Resistance also sometimes seems to weaken the virus, allowing you to keep, say, a partially effective nuke in the lineup at a lower dose while sometimes removing the PI—along with its side effects. Over time, Bellman says, some people can get by with fewer—and less toxic—meds.

LOWERING THE VOLUME: Bellman has found an immune activation "set point" that predicts whether your HIV will quickly run amok—or just amble along with no great ambitions. We don't have any great drugs capable of lowering this set point elegantly, but there are, along with HU, a handful of older immune suppressors kicking around. Immune activation is a largely neglected corner of HIV research,but fortunately, those digging there—including Bellman; Robert Gallo, MD;

and Steven Deeks, MD—are among our most creative and courageous minds. They may yet find buried treasure.

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