

ADDICTION RESEARCH

Anonymous Alcoholic Bankrolls Trial of Controversial Therapy

AMSTERDAM—For 6 years, French cardiologist Olivier Ameisen has tried to persuade addiction researchers to set up a large clinical trial of what he claims is a safe and highly effective cure for alcoholism: high doses of a decades-old muscle relaxant called baclofen.

Ameisen's main argument: his own case. There was a time when he could down a bottle of Scotch a day and, in his bestselling 2008 book *The End of My Addiction*, the cardiologist describes how baclofen broke that habit and saved his life.

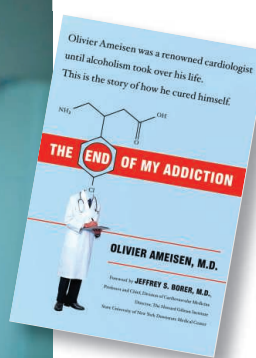
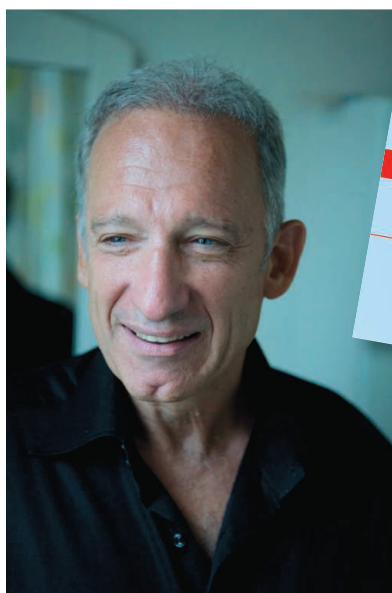
Now, Ameisen may finally get the study he wants. As a gesture of thanks to Ameisen, a Dutch donor has given the University of Amsterdam half-a-million euros to conduct a rigorous placebo-controlled study of the drug, to be led by psychopathologist and addiction researcher Reinout Wiers. The philanthropist's name is being kept secret, but Ameisen, who met him at a lecture, says the man was a "hopeless alcoholic" until he gave his physician a copy of Ameisen's book and received baclofen.

The study could help settle what Markus Heilig, clinical director of the National Institute on Alcohol Abuse and Alcoholism, calls a "controversy in a low-key way." Ameisen's advocacy for baclofen—which mimics the action of a neurotransmitter called gamma-aminobutyric acid (GABA) in the brain—has generated a lot of publicity, and increasing numbers of alcoholics demand a prescription from their doctors. But hard evidence for its efficacy has been lacking. A handful of trials have generated conflicting evidence; all were small and used much lower doses of baclofen than Ameisen recommends. The anonymous gift is a "fantastic opportunity," says alcoholism researcher Giovanni Addolorato of Catholic University of Rome.

A successful cardiologist working in Manhattan, Ameisen saw his life and career coming apart in the 1990s, when his binges frequently landed him in the emergency room. Highly motivated to kick his habit, he tried all sorts of treatments, attended thousands of Alcoholics Anonymous meetings, and checked into rehab centers. Yet he always relapsed. Then he read a story about

baclofen, a drug that in animal models of alcoholism appeared to suppress craving. He devised a study protocol in which he took escalating doses of baclofen. At 270 milligrams a day, he wrote in a rare first-person case study published in a 2005 issue of *Alcohol and Alcoholism*, "I experienced no craving or desire for alcohol for the first time in my alcoholic life." He still takes lower doses of baclofen daily to keep his anxiety in check and hasn't taken a drink since 2003.

Scientists believe that GABA may play a role in addiction, and another drug can-



Craving evidence.

In a book about his recovery (*inset*), Olivier Ameisen urged scientists to do clinical trials of baclofen.

didate for alcoholism, topiramate, also targets the GABA receptor (*Science*, 11 April 2008, p. 168). The anecdotal stories about miraculous recoveries with baclofen extend beyond addiction to alcohol to people with cocaine and other drug problems. The few randomized controlled trials—the gold standard in medicine—have shown mixed results, however.

In a study among 84 heavy drinkers with liver damage, published in *The Lancet* in 2007, Addolorato showed that 30 milligrams of baclofen a day helped 71% abstain from drinking, versus 29% of those on placebo. But in a 2010 study of the same dose among 80 diagnosed alcoholics by James Garbutt of the University of North Carolina, Chapel Hill, baclofen did not outperform placebos.

Ameisen says dosing is crucial. Another study by Addolorato's group published in April showed that alcoholics who take 60 milligrams of baclofen do better, suggesting that 30 milligrams is below the optimal dose. Ameisen says both 30 and 60 milligrams are "ridiculously low." Neurologists who use the muscle relaxant to treat spasms have long treated patients with up to 300 milligrams daily without serious side effects except sleepiness, he says.

But other scientists say it's prudent to be careful with a drug whose side effects have not been studied systematically. The U.S. Food and Drug Administration's limit for treating spasticity is 80 milligrams. The Amsterdam study now on the drawing board will escalate the dose while carefully monitoring patients, Wiers says; the researchers might put the study's ceiling at 150 or 200 milligrams. Others say that's quite high. Garbutt has proposed a new trial that would go up to 90 milligrams a day, which is "already pretty aggressive," he says. Addolorato says he would not go beyond 100 milligrams.

Ameisen is frustrated with the slow pace of research, but his zeal to convince the world is rubbing some the wrong way. "When people know all the answers before having the data, it's usually not worth listening to," Heilig says. Nor has Ameisen's treatment of skeptics—in interviews with *Science*, he described several scientists as "stupid"—made the cardiologist any friends. An adviser to the Amsterdam study, Ameisen says he's already disappointed in the communication with Wiers's team. That may be because he often fires off multiple long e-mails per day, Wiers counters.

Yet even those who are skeptical about baclofen, such as Heilig, applaud the new study because it may help bring doctors and patients some answers. The study will aim to enroll at least 200 diagnosed alcoholics, Wiers says, and will also aim to find out whether the drug is most effective in people also suffering from anxiety disorders, as some studies suggest. Functional magnetic resonance imaging will help establish whether the drug affects brain circuits involved in anxiety.

Wiers is "a highly respected investigator in the field of alcohol dependence," says Lorenzo Leggio of Brown University's Center for Alcohol and Addiction Studies. "I am sure it will be a very good study."

—MARTIN ENSERINK