

50 years ago, Clomid gave birth to the era of assisted reproduction

September 13 2017, by David Orenstein



Credit: Brown University

When Dr. Eli Adashi began practicing fertility medicine in 1974, there was nothing so revolutionary as in vitro fertilization, but at least there was the drug clomiphene citrate (Clomid). Before that came to market in 1967, Adashi said with only a little exaggeration, the job of a fertility

doctor was basically to refer couples who could not conceive a baby to adoption agencies.

"Clomiphene citrate ushered in the era of assisted reproduction," wrote Adashi, a professor of medicine at Brown University, in a new paper in *Fertility and Sterility* to mark the [drug](#)'s 50th anniversary year. "To patients whose only family-building recourse was adoption, clomiphene citrate proved nothing short of life-changing."

Still in wide use today, the drug works by modulating estrogen levels in women who are producing too much of the hormone to properly trigger a monthly ovulation cycle. There are many other causes of infertility that require other means to address, Adashi said, but by some estimates there are also millions of people, age 50 and younger, whom Clomid helped to make possible. The World Health Organization lists the drug among the globe's "essential medicines."

In the new article, Adashi, who has studied the drug in the lab and the clinic and prescribed it thousands of times over the decades, traces the drug's development, path to market and ultimate impact.

Clomid's legendary success was hardly certain, he notes. After chemist Frank Palopoli synthesized it in 1956, the William S. Merrell Company first guessed other uses for it including, ironically, as a contraceptive. Working with outside physicians, the company soon recognized it might aid fertility and launched a study, Adashi wrote. By 1961 the first clinical results appeared in the *Journal of the American Medical Association*: It restored ovulation in 28 of 36 women.

But even as Merrell was discovering and proving Clomid's value, Adashi wrote, the company could have squandered its potential with two gaping self-inflicted wounds to its credibility and balance sheet.

After incurring a 12-count federal indictment for "withholding information and making false statements" to the U.S. Food and Drug Administration (FDA) about side effects of its anti-cholesterol drug Triparanol, Merrell had to pay fines and pull it off the market. The [company](#) also distributed the notorious birth defect-causing sedative Thalidomide before the FDA provided approval, Adashi wrote. A belated recall left a cohort of severely disfigured children.

"Viewed in hindsight, it is small wonder that the regulatory adjudication of clomiphene citrate was not derailed by legal proceedings initiated against the William S. Merrell Company," Adashi wrote.

But a drug was born—and therefore, so were many children.

More information: Eli Y. Adashi, Clomiphene citrate at 50: the dawning of assisted reproduction, *Fertility and Sterility* (2017). [DOI: 10.1016/j.fertnstert.2017.08.002](https://doi.org/10.1016/j.fertnstert.2017.08.002)

Provided by Brown University

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