

# [“Effect of Vaginal Sildenafil on the Outcome of In Vitro Fertilization \(IVF\) After Multiple IVF Failures Attributed to Poor Endometrial Development” \(2002\), by Geoffrey Sher and Jeffrey Fisch](#) <sup>[1]</sup>

By: Lane, Alison Keywords: [endometrial thickness](#) <sup>[2]</sup> [nitroglycerin](#) <sup>[3]</sup> [Viagra and fertility](#) <sup>[4]</sup>

Researchers Geoffrey Sher and Jeffrey Fisch gave Viagra, also known as sildenafil, to women undergoing fertility treatment to test whether the medication could improve fertility and [pregnancy](#) <sup>[5]</sup> rates. The researchers proposed that Viagra, typically indicated to treat erectile dysfunction in men, would help women with a history of failed past fertility treatments by thickening their endometrial lining, which is the layer of tissue in the [uterus](#) <sup>[6]</sup> where an embryo implants during [pregnancy](#) <sup>[5]</sup>. Sher and Fisch gave the women Viagra during [in vitro](#) <sup>[7]</sup> [fertilization](#) <sup>[8]</sup>, or IVF, an assisted [reproductive technology](#) <sup>[9]</sup>. They summarized their findings in the article “Effect of Vaginal Sildenafil on the Outcome of In Vitro Fertilization (IVF) After Multiple IVF Failures Attributed to Poor Endometrial Development,” published in *Fertility and Sterility* in 2002. Although they noted additional research was needed, Sher and Fisch concluded that the prescribed combination treatment of Viagra and IVF resulted in an increased thickening of the [endometrium](#) <sup>[10]</sup> lining which enabled the embryo to implant and result in [apregnancy](#) <sup>[5]</sup>.

Both Sher and Fisch worked in the field of reproductive medicine prior to the study’s beginning in 1999. Sher was directly trained by [Robert Edwards](#) <sup>[11]</sup> and [Patrick Steptoe](#) <sup>[12]</sup>, who co-performed one of the first successful cases of human IVF in the United Kingdom. After Sher completed his training, in 1982, he opened one of the first private IVF clinics in the US. According to the Sher Institute of Reproductive Medicine, or SIRM, in New York City, New York, Sher had assisted in the successful [fertilization](#) <sup>[8]</sup> and births of over 18,000 IVF infants as of 2020. After Fisch completed medical school, completed a fellowship in reproductive [endocrinology](#) <sup>[13]</sup> and [infertility](#) <sup>[14]</sup> at Stanford Medical School in Palo Alto, California. He joined Sher at SIRM as the clinic’s medical director from 1999 to 2013.

In 1999, Sher and Fisch began exploring how Viagra could assist women who were having difficulty becoming pregnant or maintaining pregnancies during IVF. Viagra works by influencing the effect of nitric oxide, a molecule naturally produced by the human body that, among many functions, relaxes blood vessels by opening them wider and therefore increasing blood flow. Because endometrial growth is largely dependent on blood flow, Sher and Fisch hypothesized that Viagra could increase the growth of the endometrial lining by increasing the blood flow to the [uterus](#) <sup>[6]</sup>. A thin [endometrium](#) <sup>[10]</sup>, typically less than 6 to 8 mm thick, can reduce a woman’s chance of getting and staying pregnant, because embryos are less likely to implant or grow into a thin [endometrium](#) <sup>[10]</sup>. Preliminary data from a study published by Sher and Fisch in 2000 established the potential usage of Viagra in treating endometrial thickness for women undergoing IVF. Because that preliminary study only examined four women, Sher and Fisch then had to study a larger group of women to further investigate Viagra’s usage in IVF cycles.

Between January 1999 and July 2001, Sher and Fisch researched the effect of Viagra on [endometrium](#) <sup>[10]</sup> thickness and IVF outcome in a group of 105 infertile women. Each woman was under forty years old and had a healthy number of immature eggs that could develop into embryos. Each woman had also experienced at least two consecutive failed IVF attempts that doctors had attributed to thin endometrial lining. Because many of those previously failed attempts occurred outside of Sher and Fisch’s practice, they referenced previous medical records to supply patient histories. For the study, Sher and Fisch chose Viagra over other medications including nitric oxide, such as nitroglycerin patches, because Viagra had a lower risk of side effects. Sher and Fisch instructed the women not to take Viagra orally, but to insert it into the [vagina](#) <sup>[15]</sup> using oval shaped plastic applicators.

During the experiment, women underwent IVF treatment at Sher and Fisch’s private practice setting, SIRM clinic, in Las Vegas, Nevada. During a typical IVF cycle, healthcare practitioners perform many steps. Typically, they give a woman medication to stimulate the ovaries to produce multiple mature eggs. Then, they retrieve the mature eggs and fertilize them with [sperm](#) <sup>[16]</sup> outside of the woman’s body, after which, they transfer the fertilized embryo into her [uterus](#) <sup>[6]</sup>. During the experiment, participants took oral [birth control](#) <sup>[17]</sup> pills for ten to twenty days to establish a standard [hormone](#) <sup>[18]</sup> level. At that point, each woman began administering daily 0.5 mg leuprolide injections, also known as leuporelin or Lupron, a [hormone](#) <sup>[18]</sup> medication that prevents the premature [ovulation](#) <sup>[19]</sup> of a mature [egg](#) <sup>[20]</sup> from the ovaries. Premature [ovulation](#) <sup>[19]</sup> is a problem during an IVF cycle because it can reduce the number of mature eggs collected later for [fertilization](#) <sup>[8]</sup>. Each woman injected leuprolide once daily along with the daily [birth control](#) <sup>[17]</sup> pill, for five days. After those five days, each woman stopped taking her [birth control](#) <sup>[17]</sup> and continued the leuprolide injections until [menstruation](#) <sup>[21]</sup> began. During [menstruation](#) <sup>[21]</sup>, each woman continued daily leuprolide injections, but reduced its strength to 0.25 mg daily. When it was time to begin ovarian stimulation, each woman stopped administering the leuprolide injections altogether.

With the goal of producing multiple mature eggs, Sher and Fisch performed ovarian stimulation in multiple steps. Sher and Fisch prescribed hormonal medication called Follistim at a high dose initially, but then decreased it in half on the third day to stimulate the ovaries to develop [egg](#) <sup>[20]</sup> follicles. Egg follicles are fluid filled sacs within the ovaries that contain immature eggs. Women began taking Viagra at the same time that Follistim treatment started. Each woman inserted Viagra vaginally four times a day at a dosage of 25 mg for each insertion. The total daily dosage given to the women, 100 mg, is also the maximum recommended daily dosage for men taking Viagra. After the women completed eight days of taking Viagra and Follistim, an [ultrasound](#) <sup>[22]</sup> technician measured the endometrial thickness of each woman. Sher and Fisch then gave each woman by using [human chorionic gonadotropin](#) <sup>[23]</sup>, a [hormone](#) <sup>[18]</sup> released during [pregnancy](#) <sup>[5]</sup> to induce [ovulation](#) <sup>[19]</sup>. Sher and Fisch retrieved the resulting mature eggs thirty-five hours later and fertilized them outside of the woman's body via [intracytoplasmic sperm injection](#) <sup>[24]</sup>, a process during which a fertility specialist injects a single, healthy [sperm](#) <sup>[16]</sup> into a mature [egg](#) <sup>[20]</sup>. Sher and Fisch then transferred the resulting embryos to the [uterus](#) <sup>[6]</sup> where the embryos can embed into the [endometrium](#) <sup>[10]</sup>, creating a [viable](#) <sup>[25]</sup> [pregnancy](#) <sup>[5]</sup>.

Sher and Fisch's results from the study ultimately indicated that women treated with Viagra had thicker endometrial linings and more favorable [pregnancy](#) <sup>[5]</sup> outcomes. According to researcher Victoria Habibzadeh and colleagues, the chance of [pregnancy](#) <sup>[5]</sup> developing is higher when the endometrial thickness is between 6 to 10 mm. Out of the 105 women treated with Viagra, seventy-three women had an endometrial thickness equal to or greater than 9 mm. Sher and Fisch referred to those women as Group A. The remaining thirty-two women treated with Viagra, which Sher and Fisch called Group B, did not develop a thickened [endometrium](#) <sup>[10]</sup> lining. Group A had a significantly higher rate of successful embryo [implantation](#) <sup>[26]</sup>, despite Group B having a higher average number of embryos transferred. In Group A, thirty-three out of the seventy-three women sustained an ongoing [pregnancy](#) <sup>[5]</sup>, defined as lasting beyond sixteen weeks of [gestation](#) <sup>[27]</sup>. In comparison, zero of the thirty-two women in Group B sustained an ongoing [pregnancy](#) <sup>[5]</sup>. Sher and Fisch postulated that Viagra cannot help all women with thin endometrial linings, especially women with permanent damage to the bottom layer of the [endometrium](#) <sup>[10]</sup>, which is less likely to respond to increased uterine blood flow. Sher and Fisch state that even larger, randomized studies are needed to establish Viagra's therapeutic validity in women.

After Sher and Fisch's study, other researchers later investigated the use of Viagra in treating issues relating to female reproduction. One of those studies was conducted between 2009 and 2011 at the Research and Clinical Center for Infertility affiliated with Shahid Sadoughi University in Yazd, Iran, where researchers also examined the effect of Viagra on endometrial lining thickness and IVF outcome. Eighty women with a history of poor endometrial thickness were involved in a randomized study where they were divided into two groups. In one group, the women took Viagra, and in the other group, they took [estradiol](#) <sup>[28]</sup>, which is a sex [hormone](#) <sup>[18]</sup> that helps regulate the endometrial lining during [pregnancy](#) <sup>[5]</sup>. The researchers found that endometrial thickness and [pregnancy](#) <sup>[5]</sup> rate were higher for women in the Viagra group, although the statistical analysis showed that relationship was not statistically significant, meaning alternate factors may have caused those outcomes. However, despite some statistical uncertainties, the researchers recommend routine use of Viagra in the fertility treatment of women with a history of failed IVF attempts due to thin endometrial lining.

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## Subject

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## Topic

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