**The Devastating Effects of a 1940s Synthetic 'Wonder Pill' Haunt Women Generations Later**

**DES (Di-Ethyl-Stilbesterol)** was a form of synthetic estrogen marketed to women in the mid-20th century, and an estimated five to 10 million women took it while pregnant. The drug was later found to cause miscarriage, a neoplastic growth on their cervix + a rare form of vaginal cancer in girls.

By Amanda Arnold

In the throes of puberty, 14-year-old Su Robotti had developed "humongous breasts," but she was still waiting for what she really wanted: her period. The year was 1969, and Robotti was filled with anxiety as she watched her friends, one-by-one, come to school and report that they had begun menstruating. All the while, she kept quiet, agonizing over when she'd ruin her first pair of underwear. At times, she even considered lying about it, but nervous thoughts would always inevitably halt her—she couldn't even pretend she knew what cramps felt like.

Robotti's mother, who had gotten her period when she was 12, was less anxious and more worried. At her mother's insistence, Robotti found herself reclining in a gynecological chair. She watched as a doctor massage her lower abdomen as part of an external pelvic exam, and then listened to him deliver the report to her mother: Her reproductive organs were infant-sized and she only had one working ovary.

"I just felt like I wasn't enough," remembers Robotti today. At 59 years old, Robotti still hasn't gotten her first period—and she never will.

Robotti is a "DES daughter," born to one of the one in the estimated five to 10 million women who took the first-ever synthetic estrogen, diethylstilbestrol, while pregnant. While marketed as a drug to help prevent miscarriages, the estrogen was pervasive, winding up in everything from prenatal vitamins to
weekly shots to daily pills. Eventually, it would make its way into the blood of fetuses. When born, these children would often find themselves with abnormal reproductive organs—often causing infertility—and an elevated risk of developing various forms of cancer.

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Many, like Robotti, would also find themselves facing something that would further complicate their relationship to their bodies: an ingrained distrust of the medical community. What Foucault called the "clinical gaze," or the cognitive relativity that medical practitioners prescribe truths to their subject's bodies, is the structure on which modern medicine balances—but one that crumbles when trust is broken. For Robotti, that trust has never been there; she argues it shouldn't be there for anyone.

"I feel the need to keep [the conversation around] DES alive to try to make sure something like it will never happen again," Robotti says before adding, "though it will."

Before it was known for its toxicity, DES was heralded as "the wonder drug" for women.

In 1938, biochemists at the University of Oxford first synthesized diethylstilbestrol, a nonsteroidal estrogen that became commonly referred to as DES. And while its path to approval in the United States was not long, it was far from straightforward.

In The Retreat From Precaution, Nancy Langston writes of how DES came to enter the market. In the 1920s, scientists had discovered that both sexes produce varied levels of both "female" estrogen and "male" testosterone, fracturing the socially and politically-ingrained notion of male-female duality. Concurrently, endocrinologists were in the midst of discovering how women's hormone levels fluctuate around menstruation and menopause, which helped to institute the belief that women's hormones were the ones to be regulated. In the 1930s, doctors began the quest for a long-acting, cheap synthetic estrogen.
"Doctors soon realized...they could give hormones to smooth out and rationalize the variations in a woman's body," Langston writes. "To make women's bodies controllable and predictable—to make them fit a particular model of orderly changes—doctors and scientists joined forces." In 1941, FDA Commissioner Walter Campbell approved DES as a treatment for menopausal symptoms, postpartum lactation suppression, gonorrheal vaginitis, and atrophic vaginitis.

Much of DES's prevalence in the US can be attributed to husband-and-wife biochemists Olive Watkins Smith and George V. Smith. The couple found that women's levels of estrogen dropped right before they miscarried, so they conducted non-randomized, non-blind clinical trials of giving DES to pregnant women "who started their prenatal care in the first half of their pregnancy," according to the CDC; they figured that pumping women's bodies with synthetic estrogen was the easy solution, and according to the findings of their (poorly conducted) study, it was.

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In 1949, the team published their pro-DES results in prestigious journals like the New England Journal of Medicine and the American Journal of Obstetrics and Gynecology. Soon, physicians started flooding the bodies of their pregnant patients with the wonder drug. All the while, farmers were simultaneously giving DES to lambs, cattle, and other livestock to promote rapid weight gain.

According to Langston, reviews of research published in 1953 and 1958 found that DES did not decrease the risk of miscarriages in women; instead, it increased it.

In 1959, the FDA banned the use of DES in fattening chickens because "exposed male agricultural workers suffered sterility, impotence, and breast growth," Langston writes. But the FDA wouldn't tell doctors to stop prescribing DES to pregnant women for 12 more years.
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When Robotti was moved to a hospital in Syracuse just after hearing of her malformed anatomy, she recalls lying in a bed in a room next to a girl who had two complete sets of reproductive organs. Unlike Robotti, she had gotten her period; it was while inserting a tampon that she discovered that her body, too, felt strange.

"I remember the nurse pulling my mother aside and saying, 'This ward is full of girls with cancer and girls with reproductive abnormalities,'" she says. "It was just kind of a freak show." Upon being released from the hospital, her parents and doctors reiterated the same message: You may not be able to have biological children, but you could always adopt one day.

Despite her anatomy, Robotti can't say for a fact that she was DES-exposed. During all of her tests and procedures, her mother remembers being given weekly shots and daily pills from her obstetrician while pregnant, though she was never told what they were. When she called her doctor during her daughter's scare, he said he couldn't remember what drugs she was given, but that he was sure he would not have given her something that would hurt her
or her daughter. When she called her pharmacist, she was told that he had lost his records in a fire.

"There were a lot of doctors and pharmacists with fires that year," Robotti jokes.

The FDA urged doctors to stop prescribing DES in 1971, upon the release of a study that found DES caused clear-cell adenocarcinoma (CCA), a rare vaginal and cervical cancer, in daughters as young as seven years old. However, because use of DES was discouraged but not banned by the FDA, there were instances of doctors prescribing it past 1971.

The CDC estimates that anywhere between five and 10 million women took DES in one form or another between 1938 and 1971, though many women will never truly know, as it wasn't uncommon to be given the drug through a shot or prenatal vitamin without explanation.

While some male children, known as "DES Sons," were at risk of developing smaller-than-average sexual organs and epididymal cysts, it is the drug's effect on the daughters that is especially tragic. According to a CDC fact sheet, DES Daughters are 40 times more likely of developing CCA, a rare vaginal and cervical cancer; women over 40 are twice as likely to be diagnosed with breast cancer; infertility, ectopic pregnancies, and preterm births are more common; and more than a third today are living with identifiable genital abnormalities. Doctors today are still studying the granddaughters and grandsons of the women who took DES to see how they may be affected, though this generation is still relatively young.

While the story of DES is particularly tragic, the drug was by no means the first or the last to irreversibly damage the bodies and mental wellbeing of countless women. From the mid-1950s through early 1980s, over 30 million women worldwide took Bendectin, a combination antihistamine and vitamin B6 supplement, approved to treat morning sickness but allegedly caused birth defects. Other drugs like Yaz, a hormonal birth control pill containing drospirenone, have been proven to be harmful for some women, but apparently not harmful enough. The FDA found a 74 percent increased risk of blood clots among women taking pills with drospirenone, but it still has not mandated a Yaz recall. In 2011, the FDA asked an advisory board to review its medical risks, but according to Drug Watch, the group concluded that Yaz's
benefits outweighed it risks. More than 10,000 people have filed lawsuits against the drug's parent company, Bayer.

While some drugs that disproportionately hurt women were hormonal and intended specifically for women, others were non-hormonal and prescribed to both sexes. In her 2014 TED Talk, "Why medicine often has dangerous side effects for women," Alyson McGregor, a Brown University professor and emergency medical practitioner, cites a fact from a government accountability study: Eighty percent of the drugs withdrawn from the market are due to side effects on women. Therefore, McGregor has dedicated much of her time to studying this imbalance, which she traces back to how clinical research has been historically implemented since WWII.

"Women were considered protected subjects because they were of a childbearing age, [and] this was during a time when science was maturing and we were creating more prescription drugs," she tells Broadly. At this time, doctors didn't recognize that women's weight differences, hormonal levels, or age could affect how their bodies metabolize drugs.

In the 1960s, many women in Europe took thalidomide, a drug meant to prevent early miscarriages but that instead caused over 10,000 birth defects worldwide (DES was later nicknamed "silent thalidomide"). In partial response to this, in 1977 the FDA recommended that women of childbearing age be excluded from small-scale and early phase drug trials, as they didn't want to risk potential harm to fetuses. According to a 2001 report from the US General Accounting Office, the FDA's suggestion ultimately led to the widespread exclusion of women from nearly all clinical drug trials. Even female animals were discriminated against in biomedical research, according to multiple studies from the past five years, and their exclusion is based on many of the same assumptions that pharmaceutical companies still make today: that females' hormone cycle makes the sex a less homogenous group, and that the male subjects' reactions can be applied to females.

While DES was FDA-approved before 1977, there is little documentation of its testing on women beyond a few small scale trials. In one of the 1950s studies that illuminated the risk of miscarriage in women taking DES, researchers actually tested on pregnant women without their knowledge or consent.
By 1993, the FDA mandated that women be included in clinical studies (it should be noted that there exists no such regulation for animal studies). However, it's still not always par for the course for studies to analyze how different sexes respond to drugs, perpetuating many of the issues that existed when women weren't included in studies in the first place. While the 2001 GOA report deemed women "sufficiently represented" in clinical studies, the authors also noted that few of the drugs' analyses interpreted possible sex differences in drug safety or efficacy, even when the NDAs reported differences in how the two sexes responded to the drug. And in the past decade, medical practitioners have begun to speak out about this oversight.

"The science that informs medicine—including the prevention, diagnosis, and treatment of disease—routinely fails to consider the crucial impact of sex and gender," reads a 2014 report from the Brigham and Women's Hospital in Boston. "This happens in the earliest stages of research, when females are excluded from animal and human studies or the sex of the animals isn't stated in the published results. Once clinical trials begin, researchers frequently do not enroll adequate numbers of women or, when they do, fail to analyze or report data separately by sex."

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Aside from a dangerous coupling of laziness and sexism, much of the problem has to do with money. To get sex-differentiated results in clinical studies, there's an initial monetary cost, says McGregor. She notes that women can be more expensive to test than men, as researchers have to control where the woman is in her menstrual cycle (or if she's post-menopausal) because hormones affect how the body metabolizes a drug. The FDA also does not require sex-specific analysis in the long drug-approval process or when giving dosing recommendations, which does little to incentivize medical practitioners. However, McGregor reiterates that the outcomes of these assumptions are not slight.

"You can't just enroll men and women in the same study and have that be enough," she adds, reiterating the need for sex-based drug analyses. "We're not talking about [women] getting upset stomachs. We're talking about adverse drug reactions that kill women."
The **CDC recommends** that every year, DES daughters get a mammogram, a Pap test, and a pelvic exam—or, "regular cancer screenings," as their website reads. And now that these women range in age from their 30s to 60s, doctors are watching what menopause means for DES Daughters. At this point, they still don't really know.

When Robotti starts to talk about how there's been a link between DES-exposed women and Rheumatoid arthritis, she subconsciously starts to rub one of her knuckles. It's been swollen for a while, but she stresses that it's only one knuckle. She's ignoring this one little pain and avoiding a trip to the doctor—at least for now.

To this day, Robotti calls herself a DES Daughter, but because of her lack of her mother's medical records, she still can't say for sure that she's DES-exposed. "The true marker of [whether or not your mother was given DES] is developing CCA," she says. And, at almost 60 years old, she's coming up on another age that's associated with the scare. "At least [getting that] would be a sign," she adds facetiously.

Despite her health concerns, by no means is Robotti downtrodden. While she recognizes her stress level about "the uncertainty of her future," she's dedicated her to life to not only raising awareness around DES, but also to medical side effects generally. In 2012, she started the MedShadow Foundation, an organization centered on informing patients to inquire about both short- and long-term side effects of prescription medications, and to always inquire about other options. She's also the executive director of DES Action USA, which seeks to educate women about the drug, whether they know were exposed or are still looking for answers.

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Her objective: to get patients back in control of their own bodies. It's one that Dr. Chandler Marrs, a women's health expert, holds as well. Marrs runs the publication Hormones Matter, an online publication dedicated to advancing health research and patient knowledge, and is the creator of Lucine Health Sciences, a direct-to-patient health media and online research company. Especially with the passing of the 21st Century Cures Act, which expedites the
rate at which drugs become FDA-approved, Marrs stresses the importance of patient advocacy.

"People need to quit being quiet about health concerns and drug side effects, and say what they need and what they want," Marrs says. "One of the things that you see with patient advocacy is that a few people start saying they experience something with a drug, and then all of the sudden, you have thousands who are saying the same thing. [With] social media and the internet, nothing is behind the curtain anymore."