Diethylstilbestrol (DES) in the US [1]

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Diethylstilbestrol (DES) is an artificially created hormone [4] first synthesized in the late 1930s. Doctors widely prescribed DES first to pregnant women to prevent miscarriages, and later as an emergency contraceptive pill and to treat breast cancer. However, in 1971, physicians showed a link between DES and vaginal cancer during puberty in the children of women who had taken DES while pregnant. Consequently, the US Food and Drug Administration [5] (FDA) banned its use during pregnancy [6]. In the late 2000s, several studies showed that the grandchildren of women who had consumed DES also suffered medical issues. By the early decades of the twenty-first century, roughly ten million people in the US had been exposed to DES, and three generations of individuals had suffered medical issues due to DES exposure. Researchers class DES as an endocrine disruptor, which affects the form and function of the hormone [4] (endocrine) system.

In the early 1900s, scientists worked to isolate estrogen [7], a female sex hormone [4], and to produce it in the lab. Estrogen, or estrogen [7]-like chemicals, stimulate the female reproductive system and the development of female sex characteristics like breasts and pubic hair. Scientists said that the production of a synthetic estrogen [8] would enable them to treat hormonal problems caused by lack of estrogen [7], like various cancers and difficulty getting pregnant.

Sir Edward Charles Dodds [9] specialized in biochemistry and worked at the University of Oxford [10] in Oxford, England. His biographer and colleague, Francis Dickens, said that Dodds aimed to create artificial estrogen [7] to simulate the effects of the natural hormone [4]. In 1934, Dodds and colleagues synthesized the first artificial estrogen [7] with a chemical base almost identical to that of the natural hormone [4]. However, the compound was minimally effective and had to be administered to subjects through injection, making its widespread use unfeasible, because it required individuals to visit a physician for frequent injections.

In 1938, Dodds's lab, along with the lab of Robert Robinson at Oxford, synthesized a new synthetic estrogen [8], called stilbestrol, and soon called DES. DES acted three times more powerfully than natural estrogen [7] and was effective when subjects took it orally. Researchers produced it as a lightweight powder, and many of the male workers in the lab developed breasts due to inhaling DES. DES cost about two dollars per gram to produce, rather than the three hundred dollars to produce natural estrogen [7]. Furthermore, because DES was synthesized in a laboratory that was publically funded, the product could not be patented, further reducing its cost.

Several months after the synthesis of DES in 1938, Dodds published a paper showing that DES, when given to rats and rabbits, could prevent or end pregnancies, making it a viable [11] birth control [12] or emergency contraceptive pill. However, Dodds said that the human female reproductive cycle was too delicate to introduce foreign substances into it, and he denounced the use of DES to prevent or end pregnancies. Dodds stressed the possible cancerous effects of DES and other synthetic estrogens.

Even with early signs of problems that arose when women took DES, such as miscarriages, many people used the hormone [4] to treat a variety of hormonal problems. In 1941, the US FDA, headquartered in Silver Spring, Maryland, approved DES as a treatment for menopausal symptoms, postpartum lactation suppression, gonorrheal vaginitis, and atrophic vaginitis. That same year, physicians Charles Huggins and Clarence V. Hodges at the University of Chicago [13] in Chicago, Illinois, used DES to treat metastatic prostate cancer. Huggins won the Nobel Prize in Physiology or Medicine [14] in 1966 for his use of hormones [15] like DES to treat prostate cancer.

In 1949, scientists observed that pregnancy [6] complications, like premature birth and fetal death in the womb [16], correlated with low estrogen [7] levels in the urine of pregnant women, indicating that women with a history of miscarriages could be treated with an estrogen [7] mimic like DES to prevent those complications. Many used DES to treat what they deemed as excessive height in adolescent girls during the 1950s, and in 1960 researchers showed that DES helped treat breast cancer in postmenopausal women. Physicians around the world prescribed DES to millions of individuals.

However, the use of DES quickly became problematic, as Dodds had predicted. A 1953 study conducted by researchers at the University of Chicago [13] in Chicago, Illinois, found that the use of DES during pregnancy [6] did not prevent miscarriages. In 1970, researchers linked DES to the development of clear cell adenocarcinoma of the vagina [17] in the daughters of those women who ingested DES while pregnant. Throughout 1971, researchers published more studies that linked DES to the development of irregularities in the glands of the daughters of DES users and, in November of 1971, the FDA banned the use of
Supreme Court case. In The medical conditions caused by DES spurred many lawsuits, including 1980’s Sindell v. Abbott Laboratories, a California Supreme Court case. In Sindell, two DES daughters, Judith Sindell and Maureen Rogers, sued a group of DES manufacturers
and alleged that their mothers’ ingestion of DES caused injuries to Sindell and Rogers. They could not specify a manufacturer due to the amount of time that had passed between when their mothers ingested DES and the appearance of symptoms in Sindell and Rogers. Furthermore, their mothers had used of a generic brand. The women won their case against the drug manufacturers when the court established the precedent of market share liability, for which an entire market is responsible for a share of a settlement when the individual manufacturer cannot be identified.

Sources


17. The Leuprolide Study Group. "Leuprolide versus diethylstilbestrol for metastatic prostate cancer." *New England Journal of
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