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HIBERNATE

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BY MICHAEL WILKINSON—THE WASHINGTON POST

Jill Murphy, with her husband, Luc, at their Alexandria home, suffered fertility problems stemming from her mother's use of diethylstilbestrol, or DES.

The DES Legacy

Children of Women Given the Hormone DES Decades Ago Now Cope With Their Own—and Even Their Children's—Health Problems

by LEEZ SMITH
Washington Post Staff Writer

It is with numb precision that Chris Vanselous recounts a long succession of failed pregnancies. She miscarried six babies before the birth of her daughter, Jill, the only child to survive her mother's womb.

And for years Vanselous gave credit for that solitary healthy delivery to diethylstilbestrol, or DES, a drug that she and nearly 5 million other would-be mothers were prescribed from 1938 to 1971 under the belief that the synthetic hormone would help them build families where none seemed possible.

"My doctor told me he had the magic bullet," recalled Vanselous, 68, who was taking as many as 20 of the small red DES tablets a day when she was seven months pregnant. "He said I'd have a bigger, healthier, brighter child."

But DES did not lead to healthier babies, nor did it prevent miscarriages, according to research that began appearing in 1953. What it did lead to was a host of health problems for mother and child. Widespread use of DES on pregnant women was halted in 1971, after a study linked clear cell adenocarcinoma, a rare cancer of the cervix and vagina, to those exposed to the drug in the womb.

Other children, like Vanselous's daughter, Jill Murphy, suffered malformed reproductive or-



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gans, which would later lead to increased infertility, tubal pregnancies and miscarriage, effectively robbing many of the chance to bear their own children.

Exposure to the drug also harmed male children, who face an increased risk for epididymal cysts—non-cancerous growths on the testicles—and varicose veins on the testicles. Now, research is beginning to emerge about possible risks to a third generation—the grandchildren of women who took DES. Experts worry that many in this group—the oldest are young adults—are unaware that they were exposed to the drug and may be at risk for health complications.

Because of that concern, coupled with the public's fading memory of DES and its dangers, the Centers for Disease Control and Prevention (CDC) spent three years developing a public education campaign. Rolled out in March, the effort, known as DES Update, features a Web site (www.cdc.gov/DES) to explain the impact of the drug and disseminate the newest research to consumers and health care providers. The site also includes a component to help individuals assess their own possible exposure.

"In a sense this is a very important time in the

**Aids for DES
promised better
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ES story because our ability to ask women who took DES if they did is passing, and physicians who prescribed the drug have gone out of practice or their records are destroyed," said CDC spokeswoman Arsha L. Vanderford. "While the opportunity to find out if you were exposed is existing... the health effects are ongoing." Vaseious recalls she was sitting in a hair salon in 1971, idly flipping through a women's magazine, when she happened upon an article about DES and its newly established link to vaginal cancer.

She kept the news from her daughter for years until Jill began to menstruate, after which specialists recommended the young girl be examined for complications. Tests revealed that Jill had a malformed cervix, a common result of DES exposure. Doctors warned that she would live with a threat of vaginal cancer until her twenties. There were, as far as researchers knew, no other problems associated with the drug.

But the other risks of DES became clear in 1998 as Murphy, then 34, and her husband, Luc Murphy, began to try to have children.

Murphy repeated her mother's history of failed pregnancies. Tests revealed she has a T-shaped uterus, a classic symptom of exposure to DES. After three failed pregnancies, the Alexandria couple concluded they would have no biological children.

"I knew about the cancer but never, even as I told that I could have fertility problems," said Murphy, one of thousands of women who have filed suits against DES drug makers and won settlements since 1979. "DES took my right to have children. It took the rights of thousands of women."

While damage claims have not been easy to prove, almost every case has been settled before trial, with payouts ranging from \$50,000 to \$4 million. Publicity from these lawsuits and years of grassroots organizing by women's health groups led Congress in 1992 to create a program of research, outreach and education about DES.

Every year scientific studies reveal new repercussions of the drug, which was taken by an estimated 4.8 million women, so then exposed an estimated 4.8 million children.

To date, most of the research has focused on the troubles suffered by daughters exposed in utero. According to findings published in 2001 in the American



PHOTOS BY BILL O'LEARY—THE WASHINGTON POST

Lisa Summers, pictured above and below with her adopted 8-year-old son, Nicholas, was left unable to bear children because of her exposure to DES in the womb.

Journal of Epidemiology, these women have a higher infertility rate and are two times more likely to have a miscarriage or premature labor than unexposed women.

A study released last year by National Cancer Institute researchers showed, at least preliminarily, that DES daughters over age 40 are 2.5 times more likely to experi-

ence breast cancer than unexposed women in the same age range.

With the exception of testicular cysts, no health effects have been consistently been found in DES sons. But studies sponsored by the National Cancer Institute continue to monitor health problems, such as the risk of testicular cancer, among these men.

Third-generation children—the offspring of DES daughters and sons—are just beginning to reach the age when relevant health problems can be studied.

Research published last year by the Netherlands Cancer Institute suggests that hypospadias—a misplaced opening of the penis—occurred 20 times more frequently among third-generation sons.

Experts urge caution about the future. In laboratory studies of elderly third-generation DES-exposed mice born to DES daughter mice, an increased risk of uterine cancers, benign ovarian tumors and lymphomas were found. Third-generation male mice were shown to be at risk for certain reproductive tract tumors.

Researchers continue to look for evidence of reproductive abnormalities and cancers among third-generation DES women.

A report published in August in the *Journal of Pediatric Hematology/Oncology* suggested a possible link between a 15-year-old girl's rare case of small-cell carcinoma of the ovary and her maternal grandmother's use of DES.

Questions about DES and its possible link to sexual orientation and transgender characteristics have also emerged in the last few years. (See sidebar below.)

"It's a very interesting question and frustrating for us," said Linda Thins-Enstoft, a professor at Dartmouth Medical School who authored a paper this year on the psychosocial characteristics of men and women exposed to DES in the womb. As for "transgender mixups," she said, evidence has been "extremely rare, so we can't study it in a scientific way. It's probably one of the things we'll never know." Still, she added, "if DES had a big impact [on sexuality], we'd see it."

A Breakthrough?

It was English biochemist E. Charles Dadd who in 1938 synthesized the first orally administered synthetic estrogen. Two years later, the Food and Drug Administration (FDA) approved the drug, DES, as a treatment for menopausal symptoms.

DES started to become popular in 1947, after publication of an article by Harvard University professors George Smith and Olive Watkins Smith, who theorized that high doses of DES could prevent miscarriage.

"They couldn't have been more wrong," said Pat Cody, founder of DES Action, a nonprofit group for people exposed to the drug (www.desaction.org). "Not only did it not prevent miscarriages, but DES mothers had more of them."

The truth about DES didn't surface until 1953, when William Dieckmann, a doctor at the University of Chicago's Lying-In Hospital, conducted the first controlled, double-blind study on the use of DES during pregnancy. His conclusion: DES was ineffective against miscarriage.

"But [they] kept right on prescribing," said Cody, 80, who was put on DES two years after Dieckmann's study was published. She took the pills four times a day until her 37th week of pregnancy. In total she ingested more than 10 grams of DES—as much estrogen as is found in 500,000 of today's low-dose birth control pills, she said.

It would be nearly 16 years before the research of Arthur Herbst, a physician at Massachusetts General Hospital, linked the drug to eight rare cases of vaginal cancer in DES daughters.

The FDA responded in 1971 by issuing a bulletin to physicians. It said DES should not be prescribed for pregnant women. Paving the way for other hormone replacement therapies, DES was later used for hundreds of treatments—from prostate cancer and acne and menopause symptoms, to suppressing breast milk and stimulating livestock growth. Today it is mainly used in veterinary medicine to treat incontinence in dogs and cats.

The Next Generation

Carol Perry, 48, was 16 when she was diagnosed with clear cell adenocarcinoma. She was the 13th cancer patient linked by Herbst to DES, a drug her mother took while pregnant.

"She didn't even finish the prescription," said Perry, who had a partial hysterectomy and vaginal reconstruction in 1971, days after being examined by Herbst. "I know she feels a certain amount of guilt about taking the drug, but back then you did what your doctor told you to do. You didn't question him."

Perry, who lives in Fairfax with her husband and two adopted children, is co-chairwoman of the DES Cancer Network, a support group that links more than 300 women.

"The problem now is that a lot of doctors are telling [DES daughters] that if they've passed a certain age, they don't have to worry about cancer anymore. But we don't know what the upper age limit [for developing cancer] is."

In fact, researchers wonder if there might be a second wave of health problems as more DES daughters reach menopause. Lisa Summers, 47, of Silver Spring, learned as a 19-year-old that she'd been exposed to DES in the womb. From that time on she has made regular visits to a gynecologist specializing in DES and kept track of the research into vaginal cancers, which at that time were thought to strike women only in their teens. Today cancer is considered a particular lifelong threat for DES daughters.

But Summers, a nurse-midwife, did not know until years later that the drug would lead to her own trouble carrying a baby. It was a crushing blow. Desperate for a child, she and her husband tried in-vitro fertilization. Summers said it wasn't long before she realized she was caught in the same cycle as her mother had been.

"Here I was, trying to get pregnant, shooting myself with all kinds of drugs and hormones for which there is remarkably little research on their long-term effects," said Summers, who adopted a son eight years ago.

"The lesson here is that sometimes there are effects of drugs that we're not going to be aware of for a long time. Sometimes we expose ourselves to unknown risks, and that's perfectly reasonable to do, but DES was a drug that continued to be prescribed long after there was data to say it's not doing any good. We need to remember that."

Washington lawyer Aaron Levine has handled hundreds of lawsuits claiming damages from the drug; today he represents 120 DES plaintiffs. The courts, he said, are now grappling with whether liability should extend to third-generation injuries.

"DES was the biggest nostrum in quackery since snake oil," Levine said. "It never worked. But DES hasn't gotten the play it should have because the medical community looked the other way. They didn't want to admit the mistake they made."

Jill Murphy filed suit against Eli Lilly, once the largest distributor of DES, in 1999 and the company settled the case. The amount she won remains confidential, she said, but the money will enable her and husband to adopt a child later this year. About this Murphy is matter-of-fact: "Someone had to pay for family-building," she said.

Resources

■ CDC's DES Update: 888-232-6789, www.cdc.gov/DES

■ DES Action USA: 800-DES-9288, or www.desaction.org

■ DES Cancer Network: 800-DES-NET4, www.desancanet.org

■ DES Third Generation Network: des3gen@aol.com

■ DES Sons' International Network: 250-585-6173, <http://groups.yahoo.com/group/des-sons>

■ DES Sons Network: Contact Michael Preilick at mjpreilick@hotmail.com