DES Action® VOICE

Inside

A Focus On Diethylstilbestrol

SPRING 2017 #152

How Safe and Effective Are Bioidentical Hormone Therapies?

The popularity of bioidenticals has surged over the past decade, particularly among women with safety concerns about hormone therapy (HT) during and after menopause, such as DES Daughters. Many Daughters understandably avoid HT because of obvious concerns about the risks of taking hormones. Yet many women may not realize how little research exists on these products' safety, effectiveness, purity, strength or quality. In fact, the risks of bioidenticals are pretty much the same, or sometimes possibly greater, than taking regular FDA-approved HT products.

Bioidenticals are hormones derived from plants and/or synthetically produced or altered to have a similar chemical structure as hormones produced by the body. They may also contain FDA-approved hormone products. Bioidenticals can be ordered online or compounded at pharmacies using a healthcare provider's instructions, but the FDA does not regulate most of these products because they're considered supplements. The agency leaves regulation of compounded formulations with FDA-approved products to the states. Little to no regulation controls bioidenticals' production and distribution.

Women typically choose to use bioidenticals to manage the menopause symptoms that HT treats. Menopause causes women's bodies to make less estradiol, the estrogen responsible for maintaining bone mass and vaginal tissue. Lower estradiol levels increase risks of osteoporosis and bone fractures and often lead to vaginal atrophy. HT therefore involves taking estradiol to replace what women's bodies aren't making. Women who still have a uterus also take progesterone to reduce the risk of endometrial cancer. (Estradiol by itself can cause abnormal cell growth in women without hysterectomies.)

However, the large Women's Health Study raised concerns about HT. The study investigated HT's safety and effectiveness but was cut short because it became quickly apparent that HT increased risks of heart disease and breast cancer, though the study also found HT reduced risks of colorectal cancer, bone fracture and osteoporosis. The consensus of healthcare professionals is that women should individually assess HT's risks and benefits for their particular situation with their doctor. Unfortunately, no studies specifically look at the safety of HT in DES Daughters.

Many women concerned about HT risks have opted for bioidenticals, which include forms of estradiol, estrone and estriol estrogens plus progesterone optimized ("micronized") for better absorption. Past surveys found one of the biggest reasons women choose bioidenticals is their belief that the products are natural or made "without chemicals." Unfortunately, though, that's not the case. Even plant-derived bioidenticals are usually altered in the laboratory to make them similar to human hormones, and all of them are made up of chemicals.

The term "bioidentical" is a marketing term rather than a scientific one, explains the American

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DES Symposia A Big Success

The two symposia held in early March at Mount Holyoke and Boston University brought together some of the most influential individuals working on DES issues and research today. While in-person attendance was limited, the decision to livestream the event provoked great discussions on Facebook.

The diversity of speakers at both symposia ensured that every angle of the DES story was covered—the history, the research, the legal ramifications, and the future. At the first one, at Boston University, attorney David Fine described how the DES tragedy led to legal changes, including an extension on statutes of limitation. At the Mount Holyoke symposium the next day, attendees heard from Elizabeth Myers, the director of Special Collections at Smith College who oversees the DES Archives.

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JOIN THE CONVERSATION

New Member Benefits!

Part of our upgrade to the DES Action USA website includes a new members-only area. As a member, you'll be able to log in to the Members Area for access to:

- **Searchable Doctor Listings**—If you are looking for a DES-aware doctor in your area, you can go to the members-only searchable Doctors List and search by city, state or ZIP code. You'll find doctors' names, practice names, specialties and contact information. These listings have been created by recommendations from DES Action members.
- **VOICE Newsletter**—current and historical. The VOICE is the most popular member benefit of DES Action. Now access all 36 years of newsletters and search for any topics or articles you need. The VOICE documents the history, the science and the personal stories of DES and all of us who were exposed.
- **Attorney List**—If you're interested in getting involved in possible future DES-related litigation, we offer a list of knowledgeable attorneys DES Action members have shared with us who might be able to help.
- **Exclusive Content**—an expanding collection of articles and videos accessible only to current DES members.

And more! Update your mailing address, pay your membership dues or make a donation online.

DES Action USA on Facebook

Like DES Action USA on Facebook and follow us on Twitter to stay up to date on medical and environmental health news that affects you, your loved ones and the planet. Share your thoughts with an engaged and active community. There's a ton of information swirling online 24/7 that affects the DES population—don't let it pass you by!

Online Support Group for DES Daughters

Here is a safe place for discussing very personal issues that arise for DES Daughters. We live in the farthest reaches of the country but have developed a sense of community together, via our email listserv.

What we talk about is private—just between us—so we can feel free to raise questions on topics we aren't comfortable bringing up with others. What is amazing is the depth of knowledge in the responses.

It's a terrific resource for information and support from DES Daughters who wrestle with the effects of menopause, family relationships and medical diagnosis issues specific to DES exposure. To join the support group, send an email to: DESactionDaughters-subscribe@yahoogroups.com.

New Website Information

We're changing to a new membership program to improve our service. The big thing to know is that we've reset the passwords. The new default password is: **desUSA?&B5V**

You'll find the same great content: a searchable list of doctors, a list of lawyers, and back issues of the VOICE in flipbook and pdf formats.

Find us on Facebook twitter

MISSION STATEMENT

The mission of DES Action USA is to identify, educate, empower and advocate for DES-exposed individuals.

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Another DES? The Drug Lupron Continues to Destroy Lives

One of the most important missions of DES Action USA, in addition to providing support and resources to those affected by DES, is to continue raising awareness about the pharmaceutical disaster that has so greatly impacted the lives of DES Daughters, Sons and Grandchildren. The more people know about the DES catastrophe, the less likely—we hope—future such incidents will occur.

But as we all know, they do still occur, on a large and small scale. Similar tragedies continue to result from pharmaceutical companies' actions and the regulatory agencies that are supposed to be watching out for us don't always step in when they should. Another of these situations has been playing out over the past two decades with the drug Lupron (leuprolide). It's a common drug that DES Daughters and Granddaughters may have taken or will be asked to take at some point, so it's important to know about the awful long-term side effects of this drug.

Lupron is a hormone inhibitor originally developed by Takeda-Abbott Pharmaceuticals (TAP) to treat advanced prostate cancer. By stopping the pituitary gland's functioning, the drug decreases the amount of estrogen women receive and testosterone men receive. The FDA has also approved its use for treating endometriosis, uterine fibroids and early onset of puberty in girls under 8 and boys under 9. It's the most common drug prescribed for endometriosis and fibroids, and it's very commonly used off-label during fertility treatments to shut down the ovaries before another drug is used to stimulate egg production for an in vitro fertilization cycle. Yet it is known to cause severe birth defects and is not recommended for women planning to become pregnant. It's also been used off-label for years to increase the height of preteens by delaying puberty.

Yet the side effects of the drug can completely debilitate women and last for years. As early as 1999, the FDA received more than 7,000 adverse drug reports from women and men that described a wide range of problems: severe joint pain, difficulty breathing, severe body aches, cracking teeth, chest pain, headache, migraine, dizziness, nausea, depression, vision problems, weakness, amnesia, difficulty thinking, high blood pressure, muscular pain, bone pain, worsened asthma symptoms, abdominal pain, liver function problems, anxiety, thyroid enlargement and other problems. Between 1997 and 2009, more than 22,000 reports and 651 deaths were reported. It's not clear if all of these problems resulted from the drug, but several severe side effects have been reported over and over by those who have taken it.

A survey in 2008 found that three quarters of women taking it had memory problems, and half of women had side effects lasting more than six months, the most the company claims side effects will last. A quarter of women had been suffering more than five years. The most common severe problems are drops in bone density, leading to osteopenia (a thinning of the bones), osteoporosis, fractures and similar bone and muscle problems. And many never recover.

A recent investigation of the drug by the Center for Investigative Reporting interviewed women who took the drug as children to delay puberty. One 30-year-old had her jaw replaced at age 21 and suffers from degenerative disc disease and fibromyalgia. A 20-year-old has osteopenia, a 25-year-old has osteoporosis and a cracked spine, and a 26-year-old needed a total hip replacement.

The FDA told the reporters that the agency was in the process of conducting a "review of nervous system and psychiatric events in association with the use of [Lupron] in pediatric patients," including fatal seizures. But the FDA does not appear to be directing much energy in investigating unapproved uses of the drug or the problems being reported by thousands of women who used it for endometriosis, fibroids or fertility treatments.

The news article, published in *Kaiser Health News*, revealed that even some FDA officials and employees within the pharmaceutical company have been troubled by data on the drug's effects. Some studies submitted to the FDA during the approval process were small or poor-quality. Abbvie now manufactures the drug and paid the author of one of those studies more than $150,000 for speaking engagements about Lupron between 2013 and 2015, Kaiser reported. Yet not much is being done about these problems, and the drug continues to be frequently prescribed.

What can be done? Increased awareness, reporting any side effects you've experienced, and contacting elected representatives are a start. For more information, check out www.lupronvictimshub.com or email the site's creator, Lynne Millican, at contact@lupronvictimshub.com.

DES Symposia

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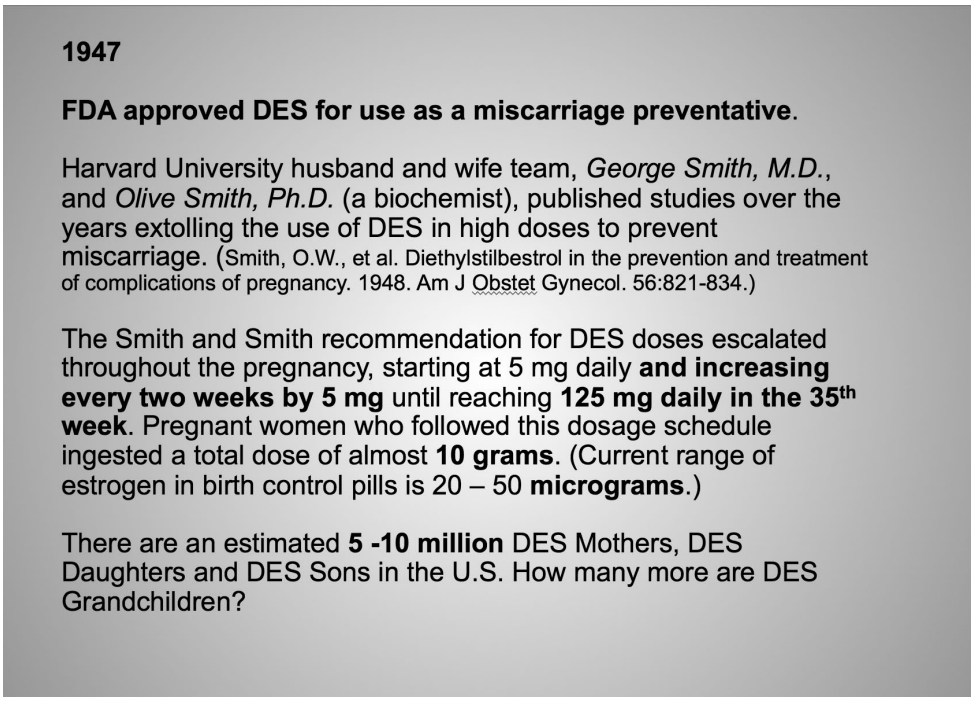
Both symposia featured talks from Su Robotti, executive director of DES Action USA, and DES Daughter Kari Christianson, a former board president of DES Action USA and a member of the National Cancer Institute's DES Follow-up Study Steering Committee. Christianson reviewed the full history of DES, from its creation as the first synthetic estrogen in 1938 by Sir Edward Charles Dodds through the discoveries of its effects and the subsequent lawsuits and advocacy that grew from forming DES Action USA. Particularly striking in Christianson's presentation—though not surprising to DES Daughters—was how little evidence existed for DES in preventing miscarriages and how long its risks were known through animal studies even as doctors still prescribed it to women.

Robotti's talk at Boston University focused on her personal story of DES exposure, and DES Daughter Karen Calechman shared her DES journey at Mount Holyoke. Also at Mount Holyoke, Robotti directed her talk to the students, urging them to turn their challenges into their passion as she did by founding MedShadow, the sister organization to DES Action that encourages people to balance



One of Kari Christianson's slides underscored just how large of a dose women received throughout their pregnancy based on the recommended regimen of DES and just how many millions suffered the consequences.

The speakers at the Mount Holyoke symposium held March 2 included Jacquelyne Luce, Marlene Fried, Kari Christianson, Julie Palmer, Karen Calechman, Su Robotti and Elizabeth Myers.

the risks against the benefits before taking medicines.

One of the most exciting aspects of the symposia involved hearing from two researchers, Dr. Linda Titus at Boston University and Dr. Julie Palmer at Mount Holyoke, who discussed interim findings of the ongoing DESAD (DES Adenocarcinoma) follow-up study. Titus is the associate director of the Hood Center for Children and Families and the principal investigator for the National Cancer Institute's DES Combined Cohort Follow-up Study. Palmer is associate director of Boston University's Slone Epidemiology Center and also a principal investigator for a study on individuals exposed to DES.

Titus and Palmer took attendees from the earliest research on the drug through the present day, when five cohorts at eight different medical centers continue to be followed. The largest of these is the DESAD cohort (started in 1975), with recent results suggesting increased risks for diabetes and heart attack in DES Daughters compared to the general population. The detailed results cannot be shared until their paper is published. Other research findings have found that DES Granddaughters appear to have a greater likelihood of irregular menstrual cycles and developing regular menstruation at a later age than their peers.

Palmer and Titus concluded by describing the future plans of the DES study at the National Cancer Institute. As the researchers continue follow-up for breast cancer and other types of cancers, they will also collect blood samples to study methylation patterns as well as hormone levels and metabolic pathways in DES Daughters. Methylation refers to the activity in DNA that can cause certain genes to be expressed or suppressed. Studying methylation can provide clues to epigenetic effects of DES, or the effects that occur across multiple generations due to changes in the genes. Future research plans also involve continuing follow-up study of DES Sons and third-generation Granddaughters to look for risk of various health conditions, including cancer. DES VOICE

Why Continue to Study DES

- Only confirmed human transplacental carcinogen
- Provides model for potential effects of endocrine disrupting chemicals, such as bisphenol A and phthalates
  - Many outcomes associated with DES are common and would have escaped detection without the dramatic increase in CCA
- Animal studies remarkably consistent with human findings
- Surveillance and monitoring of DES-exposed population for screening and health care recommendations

BU Slone Epidemiology Center

Some individuals with DES exposure history worry that attention to DES will fade away as time goes by. But too much is riding on what can be learned from DES for researchers to lose interest. No other known substance has been proven to increase cancer risk due to prenatal exposure. Understanding the biological mechanisms of DES may help identify other substances with carcinogenic potential—before they end up in a "medication." Further, as society uses more products containing endocrine disrupting compounds, findings from DES health effects may offer insight into how those substances affect human health. In addition to the obvious importance of better understanding DES effects on those exposed to the chemical, further research into DES can benefit many other people who haven't even heard of the compound. (Slide by Julie Palmer/ Linda Titus)

Other Sources of Human DES Exposure

- In U.S., 80%-95% of livestock received DES to promote growth (1950s to 1979)
- Clinical uses:
  - Excessive height in adolescent girls during the 1950s
  - Post-menopausal hormone therapy (1970s)
    - Used in charity clinics, cheaper than Premarin
  - Lactation suppression (until 1978)
  - Off-label emergency contraceptive (until early 1980s)

BU Slone Epidemiology Center

Few people may realize that more than DES Daughters and Sons have been exposed to DES. For nearly three decades, people consumed meat from the vast majority of livestock that received DES. Even as late as the 1980s, women were prescribed DES off-label as an emergency contraceptive.

DES Daughter Amy Sayers Shares Book Excerpt on DES

DES Daughter Amy Sayers traveled the painful road of infertility that many other DES Daughters have had to travel. Sayers found some healing in writing and is writing a book about her experience of learning how DES affected her and her eventual adoption of a daughter. Below we share an excerpt from her book, "Soul Rising: A Journey Through Infertility to Adoption," for which she is seeking a publisher. Her words will likely ring true for too many other DES Daughters.

For two years, I devoted myself to the process of in vitro fertilization and it took me down a black hole. I always knew I was a DES daughter, but I didn't know that birthing my own child was impossible. Back in 1996, when I had finally gotten married, my greatest desire was to have a family, and to find grace. The story is one of longing, hope, despair and magic. The outline is that of a fairy tale…

One day, while walking in the forest, a girl trips and falls. As she lies on the cold hard ground, she hears a voice whisper in her ear,

"I am the worm of past regrets."

"What do you want?" she asks.

He answers, "Give me your secrets, your shame and your lies, and I shall feel replenished."

The girl is frightened and tries to scream but her mouth freezes. Suddenly she feels her body twist and turn as the worm makes his way through her depths.

His voice hisses, "Be silent. I am here to reconfigure you."

The girl falls into a deep sleep. While she sleeps, she dreams….

Two years later, she is lying on a table in a doctor's office, hoping for the magic answer to her prayers…

…the nurse returns and brings us into the room. She tells my husband Gavin to sit in the chair next to the exam table. It feels dark and crowded in there. On the other side of the table is a screen, behind which is a dark room with medical machinery.

"Lie back and put your feet in the stirrups," says the nurse. "I'm going to prep your cervix with a little lidocaine—it might pinch a bit."

She inserts a Wallace catheter, which measures the depth of the uterine cavity. The cold metal pushing against my cervix causes my uterus to cramp. She calls for the doctor and he appears from behind the screen. He inserts the hysteroscope.

"Wow," he says. "Look at all that scarring. Have you been pregnant before?"

"Never," I answer.

"Are you a DES daughter?"

"A DES daughter? Yes, yes I am."

I feel the table quake beneath the weight of his words.

"Why? Why did you ask that?"

It was all I could do not to double over and vomit.

"Too much scarring."

"But I had surgery to remove the scarring," I protest.

As he pulls out the speculum he says, "This is very typical of DES scarring. We're talking surgery or surrogacy. This uterus will never support a pregnancy. You'll never be able to carry a child."

He pulls out the scope, takes off his gloves, and says to the nurse, "Get them over to the Surrogacy Clinic. Have them talk to Helen."

Here is what I learn when I start researching DES. My malformed uterus is not really fixable, and there is no mention of DES exposure, before or after the surgery, in my medical records. Like a worm, DES reaches into the fetus and wreaks havoc. It changes the cellular structure of feminine (and masculine) reproductive organs, weaves a webbing of scar tissue, causes clear cell adenocarcinoma, and has been linked to breast cancer as well.

This worm infects the DNA and is carried on through one generation to the next. It is common knowledge that the twisting and scarring of Fallopian tubes is characteristic of DES exposure, as was my misshapen uterus. Yet even though the research had been published as far back as the 1970s, none of the IVF doctors in 1996 mentioned DES as the source of my infertility.

Unsuccessful Fertility Treatments Linked to Heart Problems

If you've received fertility treatments but never had a child, you may have an increased risk of cardiovascular problems, found a new Canadian study. The increased risk is small but was not a statistical coincidence. Researchers looked at risk of having a large blood clot, a stroke, a ministroke, insufficient blood to the coronary arteries and heart failure. The study did not look specifically at DES exposure, but many DES Daughters experience fertility problems because of their DES exposure.

"More informed decision-making around reproductive technology requires an awareness of potential risks and the need for continued long-term clinical care," the researchers wrote in the *Canadian Medical Association Journal*. "The increased risk was particularly high among women with a prior miscarriage," they wrote, but overall risk of these events remained small. The increased risk was mostly seen in the first five years after fertility therapy.

The researchers analyzed records from 28,442 women in Ontario, Canada, who received one to five fertility treatments between 1993 and 2011. A third of these women gave birth; the others did not. Over the next five to ten years, researchers identified 2,686 cardiovascular incidents. Overall, women who received fertility therapy but did not give birth had a 21% increased risk of heart-related medical problems compared to women who gave birth. Heart failure, stroke and ministrokes were most common.

Reasons for the increased risk are complex and not fully understood, but past research findings support these findings. Researchers are exploring what preventive measures might help beyond typical recommendations, such as a healthy diet, regular physical activity and not smoking. DES VOICE

More Safety Data on Hormonal Treatments for Painful Sex

Symptoms of painful sex, low libido and vaginal dryness are usually caused by lowered levels of estrogen, which estrogen therapies can effectively treat. However, these treatments' safety specifically in DES Daughters hasn't been studied.

Now, a new study has investigated the safety of hormonal treatments for these problems in older women with breast cancer. The women were taking aromatase inhibitors, medication that can cause painful sex, reduced sex drive and vaginal dryness. The women were past menopause and had a type of breast cancer that grows due to signals sent by estrogen. The safety in those with breast cancer may be similar to the safety for DES Daughters since increased estrogen levels can affect both populations.

In the study, the women used either a cream with 1% concentration of testosterone (0.5 mg doses inserted vaginally) or an estradiol vaginal ring, which releases 7.5 micrograms of estradiol a day. The researchers tracked women's estradiol levels to see if they became elevated, defined as exceeding 10 picogram/mL, the maximum typical range after menopause.

To the researchers' surprise, just over a third of the women already had elevated levels before the study's start. These levels dropped during the study, but several possibilities could explain the initial elevation, including use of youth-enhancing skin care products that can contain estrogenic molecules not listed in the ingredients. Herbal supplements, such as evening primrose, black cohosh, red clover extract, flaxseed and wild yam, also contain estrogens.

The study results suggested that estradiol and testosterone are not risky in the short term, but the study only followed 69 women for 12 weeks. After three months, four of the 34 women (about 12%) using the testosterone cream had levels above 10 pg/mL that remained there, but none of the women using the estradiol ring did. Women in both groups reported significant improvements in their libido and less difficulty with sex and vaginal atrophy.

Adverse events occurred in 2-9% of the women, including vaginal discharge, facial hair growth, vaginal odor, vaginal itching or irritation and a urinary tract or yeast infection. Researchers couldn't conclude hormonal products are certainly "safe" because a 10 pg/mL estradiol increase is arbitrary without a comparison group. The study appeared in *JAMA Oncology*. DES VOICE

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Bioidentical Hormone Therapies

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College of Obstetricians and Gynecologists (ACOG). The hormone therapy products approved by the FDA come from both plant and animal sources and are equally "natural" as bioidentical products. The biggest difference between FDA-approved hormone therapy products and bioidenticals is that bioidenticals are unlicensed and not tested for safety or effectiveness. Unlike FDA products, bioidenticals also aren't tested for purity and consistent potency.

Women may also choose bioidenticals for their individualization. For example, a doctor may prescribe a compounded formulation instead of an FDA-approved product containing peanut oil if the woman has an allergy. Beyond these cases, however, "hormone customization is very difficult to achieve because blood hormone levels are difficult to measure and regulate accurately due to normal physiologic variations," the Endocrine Society wrote in their statement on bioidenticals.

Some providers use saliva or blood tests to assess hormone levels, but research has shown these tests are unreliable and cannot accurately measure levels. Further, the body cannot tell the difference between bioidentical hormones and ones made by the body, so tests cannot tell how much bioidenticals are absorbed. Some bioidenticals even use plant sources, such as Mexican wild yam, that produce estrogen the human body isn't capable of using. Because these levels cannot be tested and the products aren't tested, women can also received underdosage or overdosage. Overdosage can increase the risk of abnormal endometrial cell growth, endometrial cancer and blood clots.

In fact, the biggest concern with bioidenticals is safety. One survey found 71% of women believe "natural hormones" have fewer or no risks and 69% thought they had fewer or no side effects. Yet bioidenticals haven't been studied enough to show safety. Chemically, they would be expected to have the same risks as FDA-approved hormone therapies—but they aren't required to carry the same black-box warnings as FDA products, even if the risks are the same.

Neither ACOG nor the Endocrine Society say women shouldn't take bioidenticals. Both organizations emphasize the importance of informing women of the risks and lack of scientific evidence for bioidenticals' safety and effectiveness, and both call for greater regulation of these substances, especially given their continued popularity and similar risks to hormone therapy. DES VOICE