DES Action VOICE

Inside

A Focus On Diethylstilbestrol

SPRING 2009 #120

Unlocking the Mysteries of How DES Causes Harm

"Hypermethylation of HOXA 10 by *in utero* diethylstilbestrol exposure: an epigenetic mechanism for altered developmental programming," Hugh S. Taylor, et al, *Endocrinology*, March 19, 2009 as doi:10.1210/en.2009-0071.

Reviewed by Fran Howell

We know of the havoc caused by DES when introduced to a developing fetus: abnormalities of the female and male reproductive tracts, infertility problems, and cancers of the vagina, cervix and breast, among other health issues. Now, researchers at the Yale School of Medicine are zeroing in on why DES acts the way it does.

The team, led by Hugh S. Taylor, M.D., professor in the Department of Obstetrics, Gynecology & Reproductive Science, exposed pregnant mice to DES and studied their female offspring.

He was particularly interested in the HOX gene family, which regulates development. One in particular, the HOXA10 gene directs embryonic uterine development.

Earlier studies by Taylor and others have shown that prenatal DES exposure alters the process called methylation. That is how genes are switched on and off at certain times to do what they are programmed to do. The genes themselves are not changed or mutated, but rather, the way they function or express themselves is altered. DES was known to disrupt the process, but it wasn't understood exactly how.

Taylor focused on the HOXA10 genes from DES Daughter mice because they act as important regulators of tissue identity. Alterations in HOX gene expression cause abnormalities in tissues that depend on those genes for proper development.

According to Taylor, altered gene expression, or methylation, has been associated with reproductive tract abnormalities, such as those seen in DES Daughters and Sons, along with human cancers in adulthood. This research examined how HOXA10 gene expression is altered by in utero DES exposure.

What he learned is that in utero exposure to DES results in methylation of the HOXA10 gene, causing it to be lower in areas where it is normally required for uterine development and higher in areas where it should not be expressed. One of these areas is the

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U.S. Supreme Court Allows Lawsuits Against Drug Makers

Effort by DES Action USA May Have Helped

By Aaron Levine and Fran Howell

A March 4, 2009, Supreme Court ruling has major implications for those exposed to DES, because it upholds the right of individuals to sue drug companies and recover damages for their injuries.

Washington, D.C., attorney Aaron Levine, who successfully handles DES cases, says the decision "averted what might have been a disaster for DES victims still seeking compensation."

Levine filed an Amicus Brief in *Wyeth v. Levine* (no relation to Aaron Levine) on behalf of DES Action USA. It provided information for the justices to consider as they deliberated. In a nutshell, we claimed that individuals should be allowed to file lawsuits concerning FDA-approved drugs, especially if the FDA failed to rigorously evaluate the drug's safety, which is the case with DES.

In the 6-3 ruling the Court rejected drug company arguments of legal immunity for FDA-approved drugs. Therefore, DES and other product liability lawsuits can continue to be filed.

According to Levine, "the Supreme Court delivered a mighty blow to drug makers and their attempt to deny victims of dangerous drugs their day in court."

DES Action USA sincerely thanks Attorney Levine for helping present our concerns to the Supreme Court justices. The Amicus Brief gave the DES community a voice in this important decision.

DES Action VOICE

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Join OnLine Support Group for DES Daughters

Want to be in touch, via e-mail, with other DES Daughters? As a benefit of being a DES Action member you can join the DES Action Daughters On Line Support Group. That way you can ask questions and share experiences common only to those of us who are DES exposed.

To join the DES Action On Line Support Group simply send a blank e-mail to: DESactionDaughters-subscribe@yahoogroups.com

You'll receive an e-mail back from Yahoo! Groups confirming your request to join. It offers two registration options and the easiest is Option 2. Click "Reply" so the note is sent back.

Once we've checked to be sure you are a current DES Action member, you'll receive a welcome to the group letter explaining how to send messages. Then you can participate in the e-mail conversations, or just quietly read and enjoy the learning experience.

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MISSION STATEMENT

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Unlocking the Mysteries *from page 1*

vagina. This finding perhaps explains the vaginal adenosis common in DES Daughters; the HOXA10 gene is more active than it should be during development of the fetus. Reproductive tract abnormalities experienced by many DES Daughters are now suspected to be the result of lower or higher functioning of this gene.

Also noted is that the DES-caused hypermethylation of the HOXA10 gene in utero does not cease after birth. Taylor found that prenatal DES exposure "results in lasting changes in gene expression, persisting well after exposure, into adulthood." This helps explain why a developing fetus exposed to DES might develop cancers and other health issues many years after exposure.

By zeroing in on how prenatal exposure to DES causes the hypermethylation of certain genes, scientists are moving forward with a better understanding of why DES causes the problems it does, both at the time of exposure and also decades later. DES VOICE

New Internet Timeline Tool Shows Damage From Toxic Prenatal Exposures

We have come to learn that timing of toxic prenatal exposures to chemicals, like DES, is key to understanding what problems might result years later. A new Internet timeline tool offers a visual explanation of why.

Dr. Theo Colborn and her team at The Endocrine Exchange (TEDX) have developed a fascinating interactive timeline showing how the human body develops in the womb. It meticulously describes the way exposures to endocrine disrupting chemicals during development can affect health and reproduction.

Critical Windows of Development is a guide to what organs and systems are being developed throughout stages of pregnancy. It becomes clear, for example, that exposure to the endocrine disruptor Bisphenol A (BPA) during most of the First and part of the Second trimester can adversely impact development of reproductive systems, including the vagina and penis. DES is a synthetic estrogen similar to BPA, with its estrogenic properties considered even more potent than BPA's.

The site states: "Effects found in animals occur at chemical doses comparable to concentrations regularly found in humans and may provide a clue to the many disorders that have dramatically and inexplicably increased since these chemicals became part and parcel of human existence."

Although DES is not currently tracked on the timeline, more chemicals (hopefully including DES, the first known endocrine disruptor) will be added. Still, many additional links to information about DES exposure can already be found on the TEDX web site and it is worth a visit.

Dr. Colborn has long been appreciated by the DES community for her years of research on endocrine disruptors, including DES, and she is a co-author of the outstanding book, *Our Stolen Future*.

To view this informative timeline tool, visit: www.endocrinedisruption.com/home.php and click on the Critical Windows of Development link in the What's New box. DES VOICE

Our Voices Are Heard And Yogurt Is Safer

By Kari Christianson

The banner on Breast Cancer Action's web site says it all: Yoplait goes rBGH free! We did it!

In a victory for consumers, including DES Action members, General Mills announced that by August 2009 Yoplait yogurt will no longer contain milk from cows injected with the genetically engineered synthetic hormone rBGH (recombinant bovine growth hormone).

DES Action USA alerted our members in VOICE 118 to Breast Cancer Action's campaign *Tell Yoplait: Put a Lid on rBGH.* Of particular concern for women is that rBGH may stimulate naturally-occurring hormones, which could increase the risk for breast cancer.

Since the General Mills announcement, other companies have presented plans to eliminate rBGH from their yogurt products, too. For example, Dannon will eliminate rBGH by 2010. Additionally, other companies, like Wal-Mart and Fresh & Easy have either eliminated or never used rBGH in their yogurt and milk. Organic products, including milk, yogurt and cheese, have never been produced with milk from cows injected with rBGH.

So, congratulations to Breast Cancer Action and consumers across the country. Our voices and concerns were heard! DES VOICE

Informative Report and Corresponding Brochure of Interest to the DES Community

Girl, Disrupted: Hormone Disruptors and Women's Reproductive Health, A Report on the Women's Reproductive Health and the Environment Workshop; and *Hormone Disruptors and Women's Health: Reasons for Concern*

Reviewed by Kari Christianson

As a DES-exposed person, or someone who cares about DES exposure, do you ever feel that no one remembers diethylstilbestrol (DES) and our on-going health concerns? If so, it's heartening to know that scientists who study endocrine disruption and women's health use prenatal DES exposure to understand and inform their current research about hormone disruptors.

Information about DES exposure is prominently included in two new publications, which report the results of a three-day January 2008 conference of researchers specializing in issues related to hormone disruption and women's reproductive health. The conference was co-sponsored by Collaborative on Health and the Environment (CHE), the University of Florida (UF) and the University of California, San Francisco's Program on Reproductive Health and the Environment (PRHE) and was held at Commonweal, a health and environmental research institute in Bolinas, CA.

These publications provide a perfect opportunity to remind others, including our families and health care providers, that understanding DES exposure is vital in order to understand today's growing concern about endocrine disruption. (The terms "hormone disruptors" and "endocrine disruptors" have the same meaning.)

Table 1 from *Girl, Disrupted* (reproduced on page 5) lists known hormone disruptors, including DES. It offers a glimpse at the variety of products and ways we are exposed to endocrine disruptors.

Historically, scientists have studied male reproductive health effects caused by hormone disruptors. A 1996 conference of researchers developed the "testicular dysgenesis syndrome" hypothesis, which states that "hormone disruption during a key period of fetal testis development might be a common origin for multiple reproductive disorders." A new generation of research was triggered by this suggestion.

The 2008 group of 18 leading researchers specializing in hormone disruption and women's reproductive health convened to discuss the issues. The result was a scientific review found in the October 2008 issue of the journal *Fertility and Sterility*, (Crain et al.), and a push to disseminate the information to a broader audience. Members of DES Action USA are an important part of that broader audience.

The "Tragic Lessons: Fetal Origins of Adult Disease" section of *Girl, Disrupted* includes facts about how DES is vital in understanding endocrine disruption and women's health research.

"DES taught us three important lessons that can guide our investigations of other chemicals:

- "Exposure to hormone disruptors during fetal development can induce reproductive tract defects or other health impacts in the fetus, even if exposure does not affect the mother's health.
- "The risk of health impacts from exposure to hormone disruptors is especially high during prenatal development.
- "A disease induced during development might only be apparent decades later, and exposure to this one chemical could lead to multiple health risks. Girls who were exposed to DES prenatally appeared to develop normally. Only in adulthood did health impacts like uterine malformations, infertility, vaginal cancer, and breast cancer become apparent.

"These lessons continue to teach scientists about the risks of modern hormone disruptors and can help our society avoid another chemical tragedy."

The brochure, *Hormone Disruptors and Women's Health*, is packed with information about how the endocrine system works and how endocrine disruptors interfere with normal function.

"Hormones regulate a wide range of functions in our body. Hormone disruptors can interfere with these functions." The ovaries, testes (in men), pituitary, thyroid, pancreas and other parts of the body are regulated by the endocrine system, which secretes hormones into the blood as chemical messengers. "Hormones direct communication and coordination among tissues throughout the body.... Hormone disruptors can scramble messages that natural hormones transfer between cells."

Both publications list a variety of ways we all are exposed to endocrine disruptors and what we can do to support better research, prevention policies and the use of healthier products. The 36 page *Girl, Disrupted* and the summary brochure *Hormone Disruptors and Women's Health* are geared for the consumer, presenting what is known and what still needs to be learned about women's health and hormone disruptors.

Free downloads of these two publications are available at www.healthandenvironment.org/reprohealthworkshop .

Or contact CHE (www.healthandenvironment.org) for copies of the report, brochure or for more information. DES VOICE

How We Are Exposed

People can be exposed to hormone disruptors indoors and outdoors, at home, in daycare or school, and in the workplace. Hormone disruptors get into our bodies when we breathe, eat, drink, and have skin contact with them. They can be found in household products such as cosmetics, food containers, and toys. They can come from industrial pollution and cigarette smoke. Many pesticides are hormone disruptors and can end up on our food and in our drinking water. The below table provides a few examples of hormone disruptors and their sources, but more research is needed to identify all hormone disruptors and their potential health impacts.

Table 1: Examples of Hormone Disruptors

Atrazine	One of the most heavily used herbicides in the United States and widely applied to lawns, corn, and soy crops. It is banned in the European Union due to concerns of groundwater contamination.[9]
Bisphenol A (BPA)	Invented as a synthetic estrogen in 1936 and was considered for use in pharmaceuticals[10] until the more potent estrogen, diethylstilbestrol (DES), was synthesized in 1938.[11] Thus, BPA was never used as a drug. Instead, since 1957, BPA has been used to make many common products, including some plastic products such as sports bottles and baby bottles, and in the linings of cans for food and infant formula.
Cigarette Smoke *First and Secondhand*	Contains hundreds of chemicals, including some hormone disruptors. More research is needed to fully understand how cigarette smoke affects hormone function. This research is especially important because cigarette smoke is very common and because so many health problems are associated with it.
Dichloro diphenyl trichloroethane (DDT)	This insecticide was widely used in the United States until it was banned in 1972 due to toxicity.[12] DDE, a by-product from the breakdown of DDT is also harmful. DDT is still used in some other countries, often to eliminate mosquitoes associated with malaria risk.
Diethylstilbestrol (DES)	A synthetic estrogen that was first synthesized in 1938[11] and was mistakenly thought to prevent miscarriages. The drug was prescribed until the early 1970s, when its associated health risks became known. We have learned a lot about how hormone disruptors work by studying the daughters of women who took DES during pregnancy.
Dioxins	A family of compounds that are byproducts of some manufacturing and incineration processes. The uncontrolled burning of residential waste is thought to be among the largest sources of dioxins in the United States.[13] The bleaching process used to produce most paper and cotton products also releases dioxins into the environment. Because dioxins accumulate and persist in fat, a major source of exposure for humans is through contaminated foods like high-fat beef and dairy products.
Polybrominated biphenyls (PBBs)	Used as flame retardants in electrical appliances, textiles, plastic foams and other products.[14] In 1976 the manufacturing of PBBs ended in the United States after they contaminated milk supplies.[15-16]
Polychlorinated biphenyls (PCBs)	A class of compounds that were used as coolants and insulation in electrical equipment,[17] in coating of electrical wiring and for many other purposes. They were banned in the 1970s due to their toxicity.
Phthalates	A family of compounds used as a plasticizer in PVC (vinyl), cosmetics, fragrance and medical products, such as slow-release pharmaceuticals, and plastic tubing and blood bags. Some phthalates were banned from children's products in 2008.[18]
Phytoestrogens	Estrogen-like chemicals naturally found in plant foods such as beans, seeds, and grains. Soy, for example, contains the phytoestrogen genistein.[19] Even though some plants contain small amounts of naturally occurring hormone disruptors, there are many co-benefits from eating a plant-based diet.

BOOK REVIEW

DES Used To Stunt Tall Girls' Growth Described In Excellent New Book

Normal at Any Cost: Tall Girls, Short Boys, and the Medical Industry's Quest to Manipulate Height by Christine Cosgrove and Susan Cohen, Tarcher/Penguin, $26.95.

Chris Cosgrove

Reviewed by Pat Cody

Chris Cosgrove has double exposure. She is a DES Daughter who was also given the drug for five years as an adolescent. Her parents thought she might grow too tall after she grew four inches in one year in the eighth grade. A credulous physician, ignoring the fact that both her parents were tall, put her on DES and insisted she continue, even though the pills made her nauseated. This "cure" did not work — Chris is now just under six feet tall.

When Chris learned about the flip side of drugs for height management — growth hormone for "too short" boys — she got together with medical writer Susan Cohen. They have documented the false "science" and lifelong injuries done to young girls and boys by drug companies and doctors.

Normal at Any Cost makes this indictment very real by telling the individual stories of girls who were given DES and of boys subjected to growth hormone injections. With the boys comes an appalling account of how early use of pituitary glands from cadavers led in some cases to transmission of lethal Creutzfeldt-Jakob (CJD) disease, a variation of "mad cow" disease. This is a long and well-told account of medical detection, drug company aggression in pushing their products, and physician compliance in taking a turn as god.

You will not be surprised that one of the major drug companies seeking a broader market for its growth hormone Humatrope was Eli Lilly. There was sparse evidence of its effectiveness and no evidence of long term effects. (If you do not look, you will not find.)

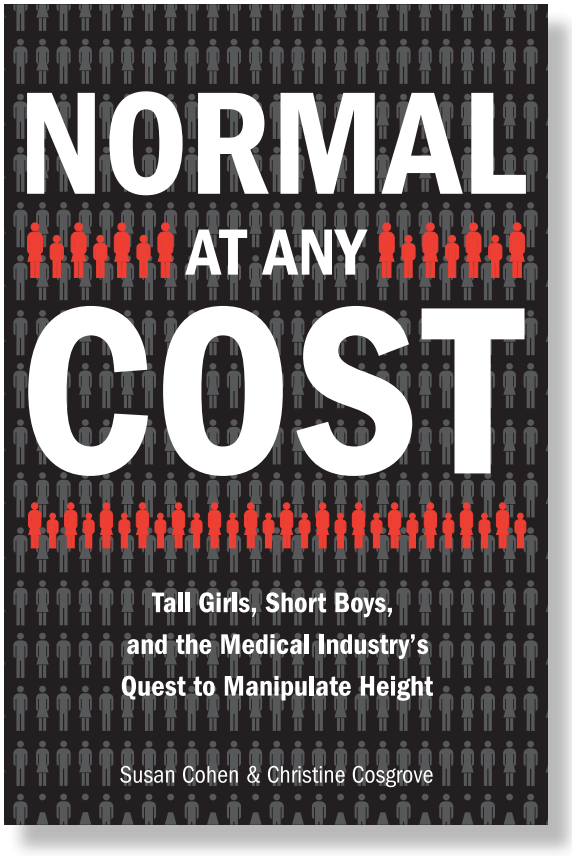
In their conclusion, Cosgrove and Cohen write:

"A half century of attempts to alter height offers some cautions: Because a treatment gives someone more of what the body produces naturally, like a hormone, does not make it safe. Because it has minor side effects in the short run, when given to a few people, doesn't mean it won't cause major illness years later or when given to a lot of people...."

On the bright side, they conclude:

"Some things do change, however. The Tall Girls grew up into societies in which being a tall woman was no longer considered a pitiable fate. The practice of giving girls estrogens for height didn't wind down because doctors reversed course, but because fewer and fewer mothers brought their daughters in for treatment...."

Normal at Any Cost resonates with all of us who were given DES as a miscarriage preventive, or who were born of these pregnancies: drug company marketing for unproven "benefits" that turned out to be non-existent, and risks still being felt today. DES VOICE



Tips From DES Daughters To Survive Hot Flashes

By Fran Howell

One thing many DES Daughters have in common is a desire to avoid extra hormone use. Therefore, hormone replacement therapy is generally avoided in favor of other menopause symptom remedies.

We had an interesting discussion on the DES Action DES Daughter On Line Support Group listserv recently. (See page 2 if you are interested in joining). Members shared ways they deal with hot flashes. It was so informative we thought others might be interested, too. With permission from those who gave us their ideas, we share some of them with you here:

I have not taken medications and don't intend to. I think exercising regularly seems to help a little. I have also reduced my caffeine intake, and that seems to make a bit of an improvement too. Finally, keeping the ceiling fan on at night has been a great thing... although my husband does not like that too much. But he is tolerating it, because it seems to really help me.

— *LANEE*

Same here! The ceiling fan has really been a help at night and I have it on all year long. I now only need it on low, and with time my "power surges" have been getting less frequent. Another thing that helped me is the "Chillow," a special water-filled pad that gave me relief.

— *SUSAN*

I try to make it to three yoga classes a week. Luckily they are taught where I work. I often miss them though, because I have to travel for my job. Not sure it is helping with the hot flashes, but it does help me feel better overall. I don't want to take any hormones. I started using black cohosh, and that seemed to help, but then I heard the reason it works is that it acts like estrogen, so I stopped. I figure the hot flashes have got to stop sooner or later, but it does seem to be going on and on.

— *JANET*

Menopausal symptoms can be greatly relieved through the use of herbs. My natural healer put together two herbal combinations to address the problems we face. One is for normal hormonal issues and the other is for surgically induced menopause. I urge you to consider herbal remedies. You can do a Google search to find a natural healer who uses herbs. I would certainly look for what type of training they've had, what type of continuing education they currently take and who they do it through. Me personally, I would look for a Certified Natural Healer, because most of them go in the direction of using herbs and foods to help people learn to heal themselves.

— *KATHY*

Lack of sleep was a huge menopause complaint. I tried everything. But over the years I've figured out that exercise EVERY DAY is key — even if it's walking the dog. VITAMINS (esp. B vitamins — I switched from Centrum regular to Centrum Silver which has a higher dosage of B complex vitamins), a well balanced diet, drinking plenty of water, no coffee after 12 noon and going to bed early (expecting 8 hours of full sleep) did the trick.

— *MOLLY*

I run a menopause group, and we compiled a long list of things to try for hot flashes. Here's a shortened version. Sometimes one thing can be the key, and I encourage you to experiment and maybe even keep a diary.

My flashes lasted for 18 months and nothing worked. They were very-scary. Now, however, five years later, when I feel one coming on, about-twice a year and always due to stress, I can consciously relax and stop it. Likewise, for insomnia, I tried a lot of things which didn't work, was miserable for four years, learned to function while exhausted, and finally things just got better.

Suggestions:

Keep cool. Slight increases in the body's core temperature can trigger-hot flashes. Wear loose clothing. Wear open neck shirts. No turtlenecks!

Sip a cold drink. Chill pillows. Take a cool shower before bed. Stick your head in the freezer at home (or in the supermarket) when a flash hits. Get to meetings early to find the best seat. Suck on hard candy. Exercise. Eat a low-fat diet. Try soy foods (in moderation) and flaxseed. Try acupuncture.

Learn your triggers. They may include spicy food, hot drinks, caffeine, alcoholic drinks, white sugar, stress, hot weather, tight clothing, hot tubs and saunas, tobacco and marijuana, anger, anxiety and stressful events or people, and even certain times of the day. If you can't avoid the stress triggers, work in a treat or some way to relax before and/or after they occur.

Find a way to see menopause as a natural transition in life, or a time with its own advantages such as greater wisdom or not caring any more what people think. Use yoga, meditation, visualization, or massage. Carry a hand massage tool with you. Practice paced respiration (deep, slow abdominal breathing) daily or when a flash starts. Practice self-validation. Get your partner and friends to tell you why you're important and why they love you.

I hope you find something helpful. I send good thoughts your way.

— *ISABEL*

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Did You Know?

DES Was Never Banned For Human Use

Time To Set The Record Straight

In 1971, after DES Daughters were diagnosed with a rare cancer, the FDA told doctors to stop prescribing DES to their pregnant patients. But the drug was NOT banned for human use.

Some doctors did not get the message, while others chose to ignore it. We are now learning of cases in which DES was prescribed well past 1971 in this country and also into the 1980s internationally.

Of note is that back in 1959, DES was banned from animal feed given to chickens and lambs after high DES levels produced side effects. They included male breast growth in humans who worked with these animals.

But DES prescriptions continued being written for women!

It wasn't until September 30, 2000, that the FDA finally withdrew its approval of DES for humans. By then, no doctors were prescribing it anyway. But DES was NEVER BANNED for human use, despite what you may have heard. DES VOICE