DES Action VOICE

Inside

A Focus On Diethylstilbestrol

WINTER 2014 #139

DES Action Health Survey

DES Sons' Responses Confirm Findings From Previous Studies

But DES Grandsons Are Still Too Young To Develop Firm Conclusions

By Deborah Wingard, Ph.D.
Professor in the Department of Family and Preventive Medicine at the University of California San Diego

In 2012, DES Action asked VOICE subscribers and other DES-exposed people to complete a questionnaire about various health problems they may have experienced (see details in VOICE issue 137, summer 2013). This article provides additional details about responses from DES Sons and DES Grandsons from the United States.

DES Sons reported many conditions already known, or suspected, to be associated with DES exposure. These conditions included birth defects and infertility. Relatively few studies report the prevalence of these conditions in DES Grandsons.

Condition	72 DES Sons	22 DES Grandsons
Undescended testicle	22%	39%
Hypospadias	14%	5%
Epididymal cysts	31%	0%
Low sperm count	31%	0%
Poor sperm quality	25%	0%
Infertility/fertility problems	24%	6%
Testicular cancer	6%	5%

As can be seen in the table, DES Sons reported most of the conditions more frequently than DES Grandsons. This may indicate that DES is more likely to have an affect on those directly exposed (DES Sons) than those indirectly exposed (their children). However DES Grandsons are still relatively young (mean age 22 years), so the prevalence of some of these conditions may increase among grandsons over time.

The most common birth defect among boys in general is cryptorchidism (an undescended testicle), occurring among 3% of full term births and 30% of premature births. Most resolve within three months and by one year of age, only 1% of boys still have an undescended testicle. Prior research has indicated that DES Sons are at increased risk of having ever had an undescended testicle. In the VOICE survey, a greater percent of DES Grandsons reported having an undescended testicle than DES Sons. This may be an artifact of small numbers (only 22 grandsons responded to the survey), or a greater number of premature births among the grandsons. Prior research has shown that their mothers (DES Daughters) are at greater risk of having premature deliveries.

The second most common birth defect among boys is hypospadias (a defect in which the opening of the urethra is on the underside of the penis), occurring in less than 1% of all male births. While DES Sons reported hypospadias more frequently than DES

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New DES Research on Bones Points to Increased Risk for Disc Degeneration

Reviewed by Kari Christianson

"Effect of *in utero* exposure to diethylstilbestrol on lumbar and femoral bone, articular cartilage, and the intervertebral disc in male and female adult mice progeny with and without swimming exercise," Sora Al Rowas et al. *Arthritis Research & Therapy* 2012, 14:R17.

A team of Canadian researchers has taken a new approach to studying the potential effects of prenatal DES exposure interference with bone, cartilage and disc growth in mice. In addition to giving different DES doses to pregnant mice over a short period of time, half of the offspring mice pups were given an exercise regiment. So, in addition to looking for DES-related changes in the musculoskeletal system, the research team wanted to see if exercise had a positive effect on DES-exposed bones.

Researcher Sora Al Rowas states, "This study aims to examine the effects of a brief *in utero* exposure to three different doses of DES on the musculoskeletal system of adult progeny, which would shed light on the possible increased risk of fracture in the sons and daughters of mothers exposed to DES during gestation, as well as in their children."

The effects of DES exposure were

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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 Online 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 Online 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.

Have You Considered Planned Giving?

Think about including DES Action USA in your estate planning, trusts and wills. Speak with your estate planning attorney to ensure your wishes are correctly put in place.

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MISSION STATEMENT

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

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DES Action Health Survey

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Grandsons, both reported it more frequently than expected. A number of international research studies have reported an increased risk of hypospadias in DES Sons and DES Grandsons, as well as animals exposed to DES. However, U.S. human studies have not found an increase in hypospadias.

Many DES Sons reported infertility, as has been reported in prior research. Few DES Grandsons reported such problems, however at a mean age of 22 years, few are likely to have been tested for infertility.

Testicular cancer was reported by DES Sons more frequently than expected (6% versus less than 1%). This may be higher than expected due to reporting bias—those with health problems are more likely to respond to surveys. Or it may reflect the higher rate of undescended testicles, known to be associated with an increased risk of cancer. Given their young age, testicular cancer was not expected among the DES Grandsons. Testicular cancer most often occurs between the ages of 20 and 39. Note, however, that the 5% reflects only one grandson out of the 22 responding, so this estimate is unstable.

These findings will be shared with the research community for more rigorous investigation, to determine if any represent a real increase or reporting bias. Without well-controlled studies, it is not possible to know if any of these conditions are truly higher than expected.

Thanks to everyone who completed the survey, which may provide clues to scientists who are investigating the long-term health consequences of DES exposure! DES VOICE

Disc Degeneration

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significant on the musculoskeletal system of the adult mice, particularly on lumbar disc bone growth. Rowas states that this study "suggests that intervertebral disc (IVD) in both male and female mice fetally exposed to DES are more susceptible to disc degeneration. Swimming ameliorated some of these effects but exaggerated others, suggesting different mechanisms of response to *in utero* exposure to DES."

DES research studies over the decades have identified a possible link to skeletal changes caused by DES exposure. Most of these studies have used the mouse model for this research, which is the case in this study. But the reason for such studies remains the same: to determine *how* DES might affect humans exposed to DES prenatally.

A 2013 research study from the NIH National Cancer Institute DES Follow-up Study found that DES Daughters and Sons reported more fractures (30% higher incidence) and osteoporosis (24% higher incidence) than unexposed study participants, suggesting an association with prenatal DES exposure. (See VOICE 136.)

Rowas suggests that this mouse study may underestimate the effects of DES, because of the brief exposure, lower doses, small animal cohort size and use of only swimming exercise. Although different DES doses were used on the mice, no dose would be considered a high dosage. DES was commonly given to pregnant women in escalating doses over weeks and months, so most DES-exposed human offspring received what is considered high dosage. While the lower doses of DES had an effect on the bones and cartilage in the mouse model, the effect of a larger DES exposure was not established by this research project.

> The effects of DES exposure were significant on the musculoskeletal system of the adult mice, particularly on lumbar disc bone growth.

However, this study suggests the need for additional study of lower dose exposures of other environmental estrogens, like BPA. And, of course, additional study of high dose DES exposure is needed to determine how and if DES affects human bones. DES VOICE

DES Daughter Toolkit Copies Now Available

DES Action DES DAUGHTER TOOLKIT

Reports coming to DES Action tell of positive responses DES Daughters are getting when they share the new **DES Daughter TOOLKIT** with their doctors.

"What a great idea! Thank you for the TOOLKIT. I gave it to my gynecologist who immediately sat down and read through it. I feel confident now that she's taking my DES concerns more seriously. I need one for my primary care doctor, too!"

With DES-knowledgeable health care providers retiring and not being replaced, it makes sense to educate the ones we use now. These providers are responding well to the accurate information from respected sources cited in the TOOLKIT. This gives DES Daughters more confidence that they are getting the specific health care they need.

Reasons for ordering additional copies:

- Misplaced original
- Have more doctors who would benefit
- Want to give copies to other DES-exposed women such as sisters, cousins and daughters

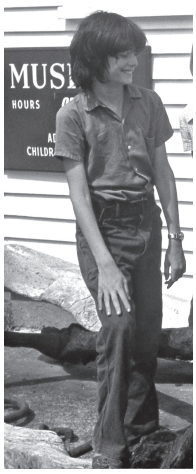
As a DES Action USA member, you received a *free* TOOLKIT in VOICE 138 (November 2013). Extra copies are available at two for $5, which includes shipping.

Send a check to DES Action USA, P.O. Box 7296, Jupiter, FL 33468.

Or order online at http://desaction.org/donate.htm and specify when ordering that you would like extra DES Daughter TOOLKITs.

LETTER TO THE EDITOR

Prenatal Hormone Exposure and Gender



I was born in New Zealand and I'm currently based in London UK. For as long as I can remember I've had a kind of partially feminine gender identity, but until recently never consciously acknowledged it. Then, a couple of years ago I realised my body language, my pattern of arousal and orgasm, and my instinctive social behaviour are all very much more like what you'd typically see in a woman rather than a man - and that I have a body that's a bit like a cross between a man's and a woman's too!

Through research I've learned this is known as a "eunuchoid habitus", and is something seen in intersex cases. I have a feminine appearance with long, slender arms and legs and a female leg to trunk ratio, described as long legs with a comparatively short upper body. Overall I look quite different from the males in my family and a lot more like my mother and sisters.

In short, I'm not just psychologically intersexed because something unusual seems to have happened to my physical development too. But what?

The sex-determining chromosome, the Y chromosome, tells our undifferentiated gonads to turn into testicles (without it they'll turn into ovaries instead). All the genetic blueprints for actually building a male or female body are located elsewhere in your genome, so everyone has the full set of instructions for both sexes.

Ordinarily this system works quite well and you'll develop as one sex throughout the pregnancy But as I now understand it, certain conditions can cause a male foetus to underproduce (or a female foetus to overproduce) testosterone causing the develping body to follow a mixture of male and female instructions.

With most intersex conditions, the abnormal hormone situation tends to be there throughout the pregnancy. In my case, there seem to have been normal male levels of testosterone to start with and towards the end of the pregnancy too, but for a period of very low testosterone in the middle.

Then I read a passage in *Brain Sex: The Real Difference Between Men and Women*, by Anne Moir and David Jessel describing a pattern of behaviour commonly shown by teenage boys who were prenatally exposed to DES. The boys were described as typically shy, socially withdrawn, lacked self esteem, were regarded as sissies, bullied, ostracised by their peers, had no ability to fight back when attacked and no interest in sport. The authors depicted it as "feminized behaviour" and it matched my teenage years so closely it could have come straight out of my school report!

DES and artificial female hormones in general are good at suppressing testosterone production in adult men. Why wouldn't they have the same effect on a male foetus? The dose of DES required to completely stop testosterone production in prostate cancer patients is 3mg per day; the starting dose for miscarriage prevention was 5mg per day.

DES Sons have the emotionally comforting knowledge that what happened to them was done to prevent miscarriage because their mothers desperately wanted and loved them. But that's not my circumstance. There was no medical reason for my mother to have been given DES and in fact, I suspect she most likely took an overdose of contraceptive pills in a failed attempt to end the pregnancy. As I see it, that could have severely disrupted my developing endocrine system so for a few weeks testoterone levels were limited. For a variety of reasons I'm fairly sure that's what happened.

Since coming to that realization I've been trying to learn as much as possible about prental hormonal disruption and I feel a kindred spirit with the DES Sons I've connected with. Many seem to share similarities with me, including genital abnormalities, feminized behavior as teenagers, endocrine issues and gender variance. Several have also mentioned having a feminine appearance, leading me to speculate that both brain development and physical appearance may be linked to prenatal hormonal exposures of varying kinds.

One thing I've noticed, though, is that many of the gender variant DES Sons I've come in contact with seem to be more psychologically female than I am, and more fully identify as women than I do. Could DES use have resulted in more male to female transexuality than would have otherwise occurred in the population? I certainly wonder.

With the growing understanding of damage caused by DES and the fact that it started serious investigation of endocrine disruption issues, I'm writing in acknowledgment that DES sparked this interest even though sadly, it did so much harm.

I thank researchers for uncovering truths and hope they continue their studies not only into DES but also into other hormones and endocrine disruptors. My situation raised questions for me and I believe the answer is in what happened before I was born. While not a DES Son, I feel a kindred spirit with individuals dealing with gender variance issues.

Sincerely,
Hugh Easton

DES Action VOICE

Behavioral and Sexual Effects?

*This commentary, by **DES Action Co-Founder Pat Cody**, was first published in DES Action VOICE Issue 104—Spring 2005. In light of the Letter to the Editor on page 4 we felt it would be interesting to re-print her wise and carefully considered thoughts.*

Over the years one of the most perplexing concerns expressed in the DES community has been whether DES exposure affected the neurological system and sexual differentiation. Our readers are aware of physical changes, such as the T-shaped uterus, the higher risk for breast cancer in mothers and daughters, and the risk for clear cell cancer in daughters. Experiments with mice show effects on the reproductive system that also appear in DES Daughters. However, reports on possible neurological effects on humans have not come from experiments but involve analyses of existing factors.

Here, some of the difficulties in getting a valid study are caused by a wide spread in the DES dosages mothers got, in the time in pregnancy when they got it, and for how long they took it. Some mothers began in the classic Smith & Smith regimen of four pills a day, increasing every two weeks until at the end—the 37th week—they were taking 125 mg. per day. This meant the DES-exposed daughter or son had DES during the critical developmental stages of his or her fetus. Other mothers had DES only in the last months, after most development had occurred and fetal life was concentrated on growth.

One 1983 research paper by Vessey et al. stated that, "sex hormones are, however, known to have effects on the organization of the brain in experimental animals with consequential behavioural effects." Another, often cited, 1982 study by Melissa Hines et al. reported that female rats exposed to DES had altered features of childhood social play and "increased masculine mounting behavior," while other researchers (Monroe and Silva) noted that same year a decrease in mounting behavior in adult male rats who had been exposed to DES.

Thus, it is apparent that DES did reach the fetal brain in these animals. In an ordinary human pregnancy, the mother's estrogen does not reach the fetal brain. We do not know if DES did reach the brain and, if it did, whether it could influence brain development. There may be protective factors in humans so that DES would not have the same effects as it has shown in lower mammals.

We have seen reports on animal models that similar environmental estrogens can significantly alter the normal biological process of sex and gender differentiation in the brain. Perhaps DES also has had these effects in humans.

Yet Theo Colborn and her collaborators, in *Our Stolen Future*, write that, "Reports linking wildlife contamination with such unexpected behaviors as females sharing nests and feminized males inevitably raise questions about human parenting and sexual choice. Could hormone disruption alter these human attributes? The science on this is slender indeed. While emerging evidence suggests that variations in sexual preference may stem from differences in biology, scientists have only a dim understanding of the factors involved…"

Our readers may recall in our Spring 2003 issue #96 we summarized an article from the *Journal of Epidemiology* on psychosexual characteristics of DES Daughters and Sons. The data came from the survey of the ongoing study group followed now at the National Cancer Institute for nearly 30 years. Questionnaires were analyzed from 3,946 DES Daughters and 1,761 unexposed women and from 1,343 Sons and 1,356 unexposed men. Results showed that 95% of the subjects, male and female, whether exposed or not, reported exclusively heterosexual partners. One percent of all respondents, exposed or not, reported "mostly same sex." On possible psychological effects, where questions were only asked of the women, 16% of the DES Daughters and 17% of non-exposed women reported diagnosis and treatment for mental illness—with depression accounting for 78% of the illnesses.

Without a doubt, more research is needed and I conclude with what a scientist once wrote, **"Absence of evidence is not evidence of absence."**

DES VOICE

French DES Health Survey Being Tabulated

More than 10,000 completed questionnaires from DES Mothers, Daughters, Sons, Granddaughters and Grandsons, along with a control group of unexposed individuals participated in the French DES survey, "Public Health: What Consequences of Distilbène?"

The high participation rate is credited to media reports and participation of 500 mutual insurance groups that publicized the federally funded project, which was run by Réseau D.E.S., the French DES consumer organization.

In France, peak years of DES prescribing were later than in the U.S., from the end of the 1960s well into the 1970s, meaning French DES Daughters are generally younger than those here. Also, usual DES doses prescribed to pregnant women in France were different from in the U.S. Therefore, researchers are eager to compare the experiences of DES exposure between both countries.

As with DES Action's Health History Survey, participants remained anonymous in France. Submissions were either by mail or Internet.

There were surprises as researchers opened envelopes. One arrived without the questionnaire and with only a note that said, "yes I took Distilene" as if to finally admit it at last. Another individual returned the completed questionnaire with a prescription and small bag holding DES pills as proof of her exposure.

Results from the French survey are expected later this year. DES VOICE

Too Close to Home

How To Limit Your Exposure to Dangerous Products

http://www.silentspring.org/tooclosetohome

If you think your home is safe from exposure to endocrine disrupting chemicals and other hazardous exposures, you may be surprised. Our friends at the Silent Spring Institute have a new website with tips for avoiding harms you probably don't realize lurk where you live.

The list is long and compelling, with items you may not have even considered dangerous. Think about your shower curtain.

"Phthalates are the plastic softeners that account for the strong odor you smell when you open up new vinyl shower curtains; over time, as phthalates leak out, the curtains tend to grow brittle. Phthalates are endocrine disrupting compounds associated with cancer, impaired fertility and male birth defects."

The website is rich with all kinds of tips for reducing our exposures to harmful ingredients in cleaning products, make-up, and household items.

We all want a clean house but have you considered what is in the products you buy? This site offers useful alternatives.

- Instead of those throw away dusting wipes try a microfiber cloth, with the benefit that you can machine wash it and reuse it over and over.
- Clean your tub without bathroom cleaners by applying vinegar on a sponge and wiping. Add baking soda as you would use scouring powder and rinse thoroughly.
- Dissolve 4 tablespoons baking soda in 1 quart warm water for cleaning counters, floors and other hard surfaces.

Those are but a few of the many suggestions you'll find at the website. If we, the DES-exposed who experienced the health and reproductive damage caused by one of the first identified endocrine disruptors, won't try to prevent further harm to our health and the environment, then who will? We can't undo DES harm, but we can make a conscious effort to change our old habits. This website gives terrific information on how to switch to safer products and practices. DES VOICE

DES Action Information For and About DES Sons

What DES Sons and their doctors should know about lifelong risks of prenatal DES exposure. This can be a starting off point for a discussion on DES Son health concerns.

DES (diethylstilbestrol) is a synthetic estrogen given as an anti-miscarriage drug to millions of pregnant women, primarily from 1938-1971, but not limited to those years. Male offspring from those pregnancies are known as DES Sons.

Increased Risk for Structural Changes

"Urogenital Abnormalities in Men Exposed to Diethylstilbestrol in Utero: A Cohort Study," Palmer et al. *Environmental Health* 2009; 8:37 (http://www.ehjournal.net/content/8/1/37)

- **Epididymal Cysts**—benign fluid filled sacs that can be painful and if so these growths may be deemed appropriate for surgical removal
- **Cryptorchidism**—undescended testicles – can result in an increased risk for *testicular cancer*—so any man with the condition, DES-exposed or not, should be vigilant about practicing testicular self-exam
- **Microphallus** (micropenis)—has no impact on fertility, although it can have pscho-social significance
- **Testicular Inflammation/Infection**—researchers speculate that some DES Sons were born with a small structural abnormality, such as a minor obstruction could explain their higher inflammation/infection risk

Infertility

"Reproductive Outcomes in Men with Prenatal Exposure to Diethylstilbestrol," Perez et al. *Fertility and Sterility;* Vol. 84, No. 6, Dec. 2005

- DES Sons are slightly more likely than unexposed men to experience infertility but most DES Sons appear able to father children
- No evidence found that infertility was greater in DES Sons with urogenital structural anomalies
- Needing further study is whether infertility issues for DES Sons increase with age

Other Medical Conditions

"Medical Conditions Among Adult Offspring Prenatally Exposed to Diethylstilbestrol," Troisi et al. *Epidemiology*; Vol. 24, No. 3, May 2013

- DES Sons join DES Daughters in this study as being at increased risk for:
  - Cardiovascular disease (stroke, coronary artery disease and heart attack)
  - Diabetes
  - Osteoporosis
  - Fractures

Gender Issues

Endocrine disruptors are being examined in gender identity studies, but DES research has not found a conclusive DES link. One confounding thought now under investigation regards the layering of endocrine disruptive exposures, both prenatally and perinatally. Researchers want to understand *if* there is an association and then whether DES exposure might itself be the cause, or perhaps combined with other exposures be a trigger for variations.

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Let's Clarify a Bit of Historical Confusion

Some reports mention that it was at Vincent Memorial Hospital in Boston where doctors first linked prenatal DES exposure to health problems. Others maintain the finding was initially associated with work done at Massachusetts General Hospital (MGH). Turns out both are correct.

Vincent Memorial was founded in 1891 and named for Boston actress Mary Ann Vincent, who was highly regarded for her charity work. The hospital had a modest start with twelve beds dedicated to the care of sick and indigent women. Seventeen years later Vincent Memorial moved to a larger facility that served its needs until officially becoming the gynecological unit of Massachusetts General Hospital in the 1940s. However, the agreement allowed Vincent to keep its name and staff in tact.

In 1947 the Vincent Memorial Hospital moved into three floors of the newly completed Vincent Burnham Building on the Massachusetts General Hospital campus where it maintained its independent status until 1988. That's when the Vincent officially gave up its independent hospital license and became the Vincent Department of Obstetrics and Gynecology.

Laying the cornerstone of the Vincent Memorial Hospital at MGH

While still officially named Vincent Memorial Hospital, researchers and clinicians there significantly moved women's reproductive health care forward. The official history states, "Some important early milestones include pioneering the routine use of the Pap smear, the identification of a relationship between polycystic ovaries and infertility, the establishment of a program to measure hormone receptors in breast cancer tissue, and the discovery of a link between gynecologic cancer in adolescent girls to their mother's use of DES during pregnancy."

Since the DES discovery was made in 1971, it technically happened at Vincent Memorial Hospital. But with that facility located at MGH and now officially incorporated into the larger hospital, most often now it is said that harm caused by prenatal DES exposure was first identified at Massachusetts General Hospital. Either way, we are thankful to the dedicated doctors and researchers who made the connection and raised the alarm about DES. DES VOICE