DES Action VOICE

Inside

A FOCUS ON DIETHYLSTILBESTROL

WINTER 2006 #107

DES Sons at Slightly Higher Risk for Infertility But Most Can Father Children

Reviewed by Fran Howell

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

This new research set out to examine reproductive outcomes for DES Sons, and the results are encouraging. While there is evidence that DES exposed men are slightly more likely to experience infertility than unexposed men, they seem to overcome the hurdle. The number of DES Sons who fathered pregnancies or live births, which were reported in this study, is the same for both DES Sons and unexposed men.

Information for the research was gathered from the National Cancer Institute's (NCI) on-going DES Follow-Up Study. Questionnaires are used to keep track of the health of known DES exposed individuals. Answers from DES Sons from the 1994 and 1997 surveys were analyzed for this investigation, which included a total of 1,085 DES Sons and 1,047 unexposed men.

Researchers are not sure why there is a slightly increased risk of infertility for DES Sons, meaning they were more likely than the unexposed to report spending more than a year trying to father a pregnancy with no success. The scientists wonder whether "differences in the tissue composition of the testis or altered sensitivity to hormonal messages due to permanent changes in gene expression" may play a part. They add that, "recent studies in mice have also shown that prenatal exposure to DES induces changes in the expression of testicular genes."

But while the researchers can't yet explain the causes for infertility problems in DES Sons, they feel comfortable about eliminating one. "We found no evidence that the association between DES and infertility was greater in the group of men who reported a urogenital anomaly," such as a varicocele, or an undescended testicle. The number of DES Sons reporting epididymal cysts on these questionnaires was quite small. In that group, the rate of infertility was

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DES Research Funding Continues!

By Kari Christianson

A major DES research project, the National Cancer Institute (NIH) DES Follow-up Study has been funded for another five years. It follows the health of more than 20,000 DES Mothers, Daughters, Sons and now Granddaughters. It's the largest scientific effort in the world regarding DES exposure. Through the years it has provided data from which much of our knowledge regarding DES has been derived.

The announcement was made by Dr. Robert Hoover, study director and Director of the NCI's Epidemiology and Biostatics Program in the Division of Cancer Epidemiology and Genetics. When he told participants on the December 5th Steering Committee conference call the good news, the excitement was palpable and a lot of verbal high-fives were exchanged by all of us on the call.

A new round of questionnaires will be mailed out this year to the DES exposed individuals whose health has been tracked beginning in the mid 1970s. Continued funding means another survey will be developed and mailed out in 2011. Scientists examine responses to determine rates of cancers, benign breast and gynecologic tumors, precancerous conditions of the cervix, autoimmune diseases, psychiatric disorders and other health issues possibly connected to DES exposure.

The response rate for past questionnaires has been consistently high, which adds to the validity of health findings by the investigators in their analyses of the data. This high rate of response is one of the strong "selling points" within the National Institutes of Health for continuing this large cohort-based research.

Dr. Hoover offered a grateful

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Join On Line Support Groups for DES Daughters or Sons

Want to be in touch, via e-mail, with other DES exposed individuals? As a benefit of being a DES Action member you can join either the DES Action Daughters On Line Support Group, or the one for Sons. 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

To join the DES Action Sons On Line Support Group simply send a blank e-mail to:
DESactionSons-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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DES Sons *from page 1*

somewhat higher among DES Sons, however, because of the small number in that group it was not possible to make any determination about that.

One thing to note is that the researchers saw enough in their analysis to wonder whether DES affects fertility as men age. "Although speculative, our data may reflect an increased effect of DES on infertility with advancing age." It is something that requires additional study.

"Although speculative, our data may reflect an increased effect of DES on infertility with advancing age." It is something that requires additional study.

What researchers were able to discern is that there seems to be no correlation between dose and timing of DES exposure on fertility outcomes. They examined low dose and high dose statistics, as well as timing of initial exposure across the group. Their finding is that it made no difference on the mean number of pregnancies or live births in the subset of men who reported ever fathering a pregnancy.

Although the scientists had no information about partners of the participants in this study, they feel it is unlikely that the partner's fertility status would differ for the DES-exposed and unexposed men in such a large group.

This study was strictly on the numbers of live births, and the time it took to achieve them. It did not examine possible health issues for the DES Grandchildren who were born.

The next NCI DES Follow Up Study questionnaires will go out later this year, providing researchers with updated information on all areas of DES health inquiry.

DES Research Funding *from page 1*

"thank you" to the Principal Investigators at research sites around the country who are involved in this project. He credits their fine work, and their belt-tightening budget proposals, for the continuation of this study.

"We want to add our thanks to these dedicated researchers, clinicians, and educators who understand the consequences of DES exposure and who continue to reveal its health ramifications," says DES Action Co-Founder Pat Cody. She adds, "a special 'thank you' goes to the study participants who diligently fill out a health survey every few years to provide answers for all of us."

Also doing well is the new web site developed for the project. It generates an average of 600 hits a month since going on line. The web site is an excellent resource for the DES community and can be accessed at www.DESfollowupstudy.org. We have a link to it on DES Action's site, www.desaction.org.

Des Action is at the Table for Talks on Future Directions in Research

By Kari Christianson

At the end of November DES Action was invited to attend a meeting of the Public Interest Liaison Group (PILG) of the National Institute of Environmental Health Sciences (NIEHS) to meet the new Director, David A. Schwartz, M.D.

PILG members represent organizations directly affected by the mission and research of NIEHS. (The web address for the NIEHS PILG with links to all the public interest organizations, including DES Action, is: www.niehs.nih.gov/drcpt/pilg/home.htm).

Dr. Schwartz used this meeting to introduce a new vision for the NIEHS, which he envisions as using the environmental sciences to understand and improve human health. He stressed the need to improve the integrative and clinical work of the NIEHS in order to apply basic science to public health.

In response to the request for comments, DES Action included these remarks in our written response to Dr. Schwartz and the NIEHS:

. . . The DES-exposed populations in the United States and the world . . . are very interested in and in many ways dependent upon the groundbreaking research of the NIEHS for growth in the understanding of the health outcomes of exposure to diethylstilbestrol (DES).

Many of the goals outlined in the Strategic Plan seem to support our ongoing concerns about DES research. Particularly, goals and objectives emphasizing epigenetic influences on human health are very positive for our concerns. The goals stated for understanding human health through environmental research (of which DES and other estrogenic compounds have been a part for decades), integrative research and biomarkers are all aspects of our advocacy for additional research.

. . .we are well aware that our place in environmental health research is not a fast research find. We are hopeful that persistence continues to be one of the hallmarks of NIEHS research. . .

However, as people living with long-term and often slowly materializing health outcomes, we are well aware that our place in environmental health research is not a fast research find. We are hopeful that persistence continues to be one of the hallmarks of NIEHS research. . . .

ASK *the* EXPERT

Something new for our *DES Daughters On Line Support Group* is an *Ask The Expert* session, which we'll do from time to time with a variety of experts. The first one featured respected women's health care provider **Candy Tedeschi, NP**, who is on the DES Action Board of Directors and is well known for her more than two decades of work with DES exposed individuals.

She was on the steering committee for the CDC's DES education project (CDC's DES Update) and lectured many times around the country for that effort. She participates in National Institutes of Health conferences on DES and has been involved with several studies regarding DES Daughters. Tedeschi has written articles and lectured extensively about DES, to both the general population and to the medical and nursing communities.

Many of the questions were ones you might ask, so we thought we'd share some of what we learned.

If you are a DES Daughter, and a DES Action member, please consider joining our *On Line Support Group*. See page 2 for easy directions.

Q Is it possible to have impacts from DES such as infertility, premature labor, breast cancer, etc., (except for clear cell cancer) but not have any of the classic physical/ structural markers of DES?

A DES Daughters are all different. Classic signs of DES exposure are adenosis (glandular cells which are normally on the cervix in non exposed women but can cover the entire cervix and extend onto the vagina in DES exposed), and structural changes, i.e., cockscomb cervix, ridges, hoods, and pseudopolyp. Adenosis and structural changes often resolve over time. Keep in mind not all DES Daughters have these tissue/structural changes. Studies in the past have shown many DES Daughters have these changes but as the DES population ages we see less and less of them. I would say most DES Daughters have no visible or even colposcopic changes left by the time they are in their mid 40's. I have women who are in their 40's come into my office and ask if they have any DES changes, or if I can tell them for sure that they are DES exposed. In most cases from that age group there is no way see DES exposure, but it does not mean they didn't have adenosis or structural changes in the past that their bodies resolved over time.

Q Do DES Daughters tend to enter menopause at an earlier age? Do DES Daughters tend to have more severe symptoms during menopause and is our menopause faster or shorter than non-DES exposed women.

A The DES National Institutes of Health project is currently studying this question and we are all anxiously awaiting the answer. From what I understand the data is in but has not been published yet. Hopefully soon. From my practice I would have to say that DES Daughters probably go through menopause slightly earlier but not years earlier. I don't have data to support this but it is just my general impression. My practice includes DES and non-DES women and I haven't found the symptoms of menopause or perimenopause differ in severity or length. The difference I do see though, is non-DES exposed women are more apt to ask for hormones to help with their symptoms while DES Daughters muddle through.

Q What is the current scoop about HRT and DES Daughters if their menopausal symptoms are unbearable and they need hormonal assistance?

A While most DES Daughters like to avoid hormones, they are sometimes necessary. I have seen women who cannot function without hormones. I tend to use natural estrogens and progesterone in the lowest effective dose

for the shortest time possible.

Q My gynecologist, who is familiar with DES, wasn't aware of the DES vaginal exam so I recently explained that to him. He did a colposcopy and said everything looked good. He thinks I only need to be thoroughly examined every 2 years or so. He said next time I go for my annual Pap to make sure to remind him to swipe the vaginal walls. Am I doing enough? I'm 44 years old and not planning on any more children. My previous history includes positive Paps and subsequent freezing, miscarriages and early delivery (and now breast cancer).

A I'll start your answer with a question. What did the doctor mean when he said "everything looked good?" Do you have adenosis? Are all of your DES changes gone? I know you said you had abnormal Paps in the past that were treated with freezing (cryo therapy) but I have seen women who have their cervices treated but they still have vaginal DES changes (adenosis and metaplasia which is a normal cell change process). Freezing will obliterate the abnormal cell change and any other tissue in the area that it touches, but not surrounding areas. Ask your doctor to explain what he saw. Since you are DES exposed, current recommendations are that you need yearly Pap smears for the foreseeable future. What the doctor probably meant by a thorough exam every 2 years is having a colposcopy every 2 years. If you have had normal Paps for the last three years and your Colposcopy showed no abnormalities, having a colpo every 2 years is fine, but you still need yearly Paps. Annual exams should also include breast exams by your health care professional.

Editor's Note: E-mail us at desaction@columbus.rr.com or send a self-addressed stamped envelope to the office, and request a copy of the fact sheet that describes a proper DES exam. Then give it to your doctor to keep in your file. That way you can feel more confident you are getting the medical care you need.

Q Is there a best "time of the month" to do: breast self-exams, mammograms, pap smears? Meaning a time in our cycles during which any suspicious masses/problems could be caught? And is there a worst time, meaning one in which very little could be found, or problems be masked?

A There is less hormonal influence on our breasts, uterus and ovaries just after our periods — making days 5-10 of the menstrual cycle the ideal time for breast exam, mammography or pap smears. The worst time for breast exams and mammograms is just before our periods, as they tend to be "more lumpy" and tender. Pap smears can be done anytime during the cycle, except when you are bleeding, but ideally at midcycle. Worst time — probably during your period.

Q If you were never able to get pregnant, are your chances of reproductive cancers increased? Does never being pregnant lead to an earlier menopause than those who were able to conceive and give birth?

A To answer the second question first — no it does not lead to an earlier menopause. Never being pregnant does seem to increase your risks for reproductive cancers. The more years women menstruate and ovulate seem to increase the risk of ovarian cancer but I don't know exactly how much. Breast tissue goes through a final maturation with pregnancy, and women who do not achieve pregnancy, or who get pregnant after age 35, have a higher risk for developing breast cancer.

Q What are the chances of getting clear cell adenocarcinoma after age 48?

A The overall risk of developing clear cell adenocarcinoma (CCA) is about 1 in 1000. The highest risk period for developing CCA in DES Daughters were the teenage years and early 20's, but we have continued to see cases develop in women into their late 40's. The number of cases of CCA has been small but still there. CCA is a type of cancer that we usually see in non-DES exposed women ages 50 or older. DES Daughters in great numbers are now entering this age group and we have no idea whether DES Daughters are going to be the same or at increased risk as they age. The take home message is DES Daughters have no age at which they are not at risk for developing CCA. So don't miss your annual Pap.

Q Is there a higher incidence of benign tumors located on our internal organs? For example I have a benign cyst on my liver.

A I have not seen that problem studied. Most of us don't have routine sonograms on our abdomen so the true incidence of benign cysts is probably unknown.

Want To Share Your Story?

DES Daughter Sherry Weinman wrote the first Your Voice column, printed in our fall Voice newsletter. It was well received, with such comments as: "*Sherry's story hit a personal note for me…I realized how much DES had impacted my life and the choices I made.*" Another member wrote to say she likes "*articles that give scientific information and ones that talk about positive ways to cope…I would rather focus on what I can control and fix…*"

Now it's your turn. If you have a DES story that shows the spirit of our members who are living good lives in spite of, and with, DES exposure, we'd like to hear it.

Just email your idea, outline or completed story to: Board Member Ann Giblin at Ann@WinterlakeAssoc.com, putting DES Your Voice in the subject line. Or mail it to DES Action, 158 S. Stanwood Rd., Columbus, OH 43209. Ann will get back to you to discuss your story. We hope to hear from you soon!

DES Action T-shirts are a hit with the whole family. Fran Howell's daughter Shelby, and husband Kevin wear theirs proudly. Shelby redesigned hers with a few scissor snips at the collar to make it completely teen trendy. You can order yours by sending a check for $15 to DES Action and telling us whether you want size S, M, L or XL.

Endocrine Disruptor Studies Show Prenatal Exposure May Lead to Male Reproductive Tract Anomolies

Reviewed by Pat Cody

Our exposure to DES makes us an early group of humans affected by what we now call endocrine disruption. Lessons learned from our experiences are raising awareness about the dangers of environmental pollutants and serving as models for studying them.

A new study shows how a synthetic chemical, acting as a weak estrogen, can cause developmental change. This type of research is useful as it provides information on how endocrine disruptors, like DES, affect our health.

"Decrease in anogenital distance among male infants with prenatal phthalate exposure," by Shanna Swan et al, *Environmental Health Perspectives* June 1, 2005 (available at http://dx.doi.org/)

Phthalates, found in many plastics, and one of the most abundant man-made pollutants in our environment, enter our bodies in many ways, and can be found in our water, our food and our home environments.

This paper found a shortening of the distance from the anus to the genitals (AGD) in boys with higher prenatal exposure to phthalates. In rodents phthalates cause a range of genital changes, including shorter AGD, which are together referred to as the phthalate syndrome. This paper is the first to identify some of the same changes in humans.

The researchers examined 134 male children ages 2 – 30 months to get genital measurements. They then analyzed prenatal urine samples from 85 mothers of these boys to measure levels of nine phthalate metabolites. Their findings are consistent with those seen in studies on rats: an association between higher phthalate levels and AGD, and shorter AGD associated with less complete testicular descent. In both rodents and humans undescended testicles (cryptorchidism) is associated with decreased fertility and testicular cancer.

The authors conclude, "This is the first study to look at subtle patterns of genital morphology (development) in humans in relation to any prenatal exposure…We report that anogenital distance, the most sensitive marker of anti-androgen action in toxicologic studies, is shortened in boys whose mothers had elevated prenatal phthalate exposure.

Our Mothers Are Special

This Mother's Day do something really meaningful!

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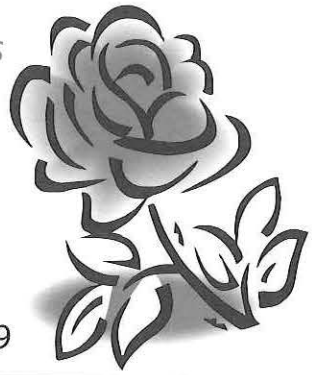

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The DES Tragedy: *Why Drug Advertising Must Change*

For many years DES Action has voiced concern about false or misleading drug advertising that results in harmful health situations, not unlike the issue of DES exposure itself. DES Action is a founding member of Prevention First, a coalition of independent health organizations in the United States and Canada that works to shift the emphasis in disease prevention away from drugs and promotes a greater awareness of the Precautionary Principle in health. Goals of this coalition include building public awareness of the pervasive nature of pharmaceutical advertising and countering false or misleading advertising about prescription drugs.

The following Opinion Piece was written by our DES Action Canada colleague, Ellen Reynolds, and was previously printed in the Canadian Women's Health Network magazine (Fall 2005, Vol 8, No. 1/2) and ran on Rabble.ca.

by Ellen Reynolds
June 27, 2005

It seems that even when we *do* know history, we're destined to repeat it.

In 1948, diethylstilbestrol (DES) was advertised only in medical journals as the "wonder drug" recommended for all pregnancies. The smiling face of a cherubic infant peered out next to the caption "Really? Yes, desPLEX to prevent abortion, miscarriage and premature labor...bigger and stronger babies too."

Advertising works. It worked for DES, which was advertised only to doctors, resulting in an estimated 200,000 to 400,000 prescriptions for pregnant women in Canada, and an estimated 4.8 million prescriptions for American women between 1941 and 1971. Despite scientific evidence from 1953 that proved DES did not prevent miscarriage, this harmful drug was advertised and prescribed for 18 more years.

Only after it was linked to cancer in the daughters of women prescribed DES was it finally restricted for use in pregnancy. Those exposed to DES continue to face the effects of infertility, reproductive abnormalities, cancer and other health problems decades after initial exposure.

But that was over 30 years ago. Surely we've learned that prescription drug advertising needs careful regulation. Apparently not.

We only have to look at recent news surrounding the arthritis drug Vioxx that is credited with causing thousands of extra heart attack deaths. During its five years on the market, its manufacturer, Merck, spent about $500 million advertising the drug to the U.S. public. Vioxx was no more effective than other similar drugs to treat arthritis symptoms, but it was a lot more expensive, and turned out to be much less safe.

It's time to remember the DES legacy, including the lesson that prescription drug marketing cannot continue to upstage science.

Back in the '50s and '60s, doctors were targets for most drug advertising. Direct-to-consumer advertising of prescription drugs wasn't permitted. We can only imagine how many more people would have been exposed to DES if it had been promoted on television, billboards, bus shelters, newspapers and magazines as prescription drugs are today.

Advertising is an effective business tool. It sells products. More is spent on it than on drug research and development. But prescription drug ads are often misleading. They downplay risks and exaggerate benefits.

Let's call a spade a shovel and quit heaping illegal advertising down the throats of consumers. Let's take our cue from most other industrialized nations, where direct-to-consumer advertising continues to be illegal. Look to the European Parliament where an attempt to introduce direct-to-consumer advertising in 2002 was soundly rejected in the name of public health. When will Canadian and U.S. regulators come to the same logical conclusion?

While direct to consumer advertising is illegal in Canada, it happens all the time because Health Canada is not adequately enforcing the law. Drug makers are taking advantage of the situation.

It's time to put the brakes on direct to consumer marketing, or else the terrible history of drug tragedies like DES and Vioxx will most certainly be repeated.

http://www.rabble.ca/news_full_story.shtml?x=40120

Ellen Reynolds is project coordinator at DES Action Canada and lives in Victoria, B.C. With background from Dr. Barbara Mintzes, drug researcher and vice-president of DES Action Canada.

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DES Daughter Leads the Way Toward a Healthier World

By Fran Howell

We don't know if members of the New York City Council saw Judith Helfand's movie, *Blue* Vinyl[1] before they voted in December to reduce the city's purchases of hazardous products, but it's entirely possible. Her film describes the dangers of polyvinyl chloride (PVC) plastic, which is used for many things, from siding for houses, to components of cars, computers, medical equipment and even children's toys.

As a DES Daughter who survived clear cell adenocarcinoma and told her story in *A Healthy Baby Girl*[2], Helfand's second movie describes how chemicals released from PVC get into our air, water and food. During production, PVC plastic releases dioxins that can cause cancer and harm both immune and reproductive systems. Meanwhile, studies show phthalates migrate out of PVC consumer products and expose us to toxic chemicals responsible for reproductive problems, among other health issues (see Endocrine Disruption article, page 6).

To check for PVCs, look for the number "3", "PVC" or the letter, "V" inside or underneath the universal recycling symbol on products. Also, soft flexible PVC products often have a distinct smell, like vinyl shower curtains.

Helfand's independent film is part of a growing education effort warning of the dangers of hazardous products. In addition to limiting purchases of PVC plastic by the city, NYC lawmakers also mandated a reduction in the city's use of products containing lead, mercury and toxic flame-retardants. Since the NYC government spends about $11 billion a year, it's hoped this move away from hazardous materials will encourage producers to make more environmentally friendly products.

The emphasis on healthy purchasing is growing. New York City joins Boston, Seattle, San Francisco and Buffalo in passing policies that limit the hazardous products those cities can buy and use.

Corporations are also joining the movement to find substitutes for hazardous PVC products. Recently, Microsoft, Johnson and Johnson, Crabtree & Evelyn, Wal-Mart, Hewlett Packard, Kaiser Permanente, Catholic Healthcare West, Firestone Building Products, and Shaw Industries began looking for ways to phase out PVCs in their products and packaging. [3]

[1] *Blue Vinyl http://www.bluevinyl.org/*
[2] *A Heathy Baby Girl http://www.itvs.org/external/babyg/hbgmain.html*
[3] *Center for Health, Environment and Justice http://www.besafenet.com/pvc/*