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A Focus On Diethylstilbestrol

FALL 2009 #122

Review of Research On DES Sons Provides Insights

Dose and Timing Matter

"Urogenital Abnormalities in Men Exposed to Diethylstilbestrol in utero: A Cohort Study," Julie R. Palmer, et al, Environmental Health 2009, 8:37-1-6, 2009 (http://www.ehjournal.net/content/8/1/37).

Reviewed by Retha Newbold

Developmental and Reproductive Researcher Emeritus, National Institute of Environmental Health Sciences

A recently published paper in *Environmental Health* by Palmer et al. reports an association of prenatal exposure to DES with an increased risk of male urogenital abnormalities

such as cryptorchid (retained) testes, epididymal cysts, and testicular inflammation. The association was strongest if treatment started before the 11th week of pregnancy and occurred at cumulative exposures of 5 or more grams of DES.

Although urogenital abnormalities have been previously reported in sons of women who participated in a randomized trial of DES at the University of Chicago in the 1950s and in a second group who were the sons of women who had been treated at a private infertility practice near Boston between 1943 and 1975, the significance of these findings

have remained unclear because similar findings were not seen in a third cohort of men whose mothers were identified as DES exposed at the Mayo Clinic from 1939-1962. Also troubling, the Mayo Clinic findings were in disagreement with DES studies in experimental animal mod-

The current report confirms that prenatal DES Sons have a higher occurrence of retained testes, testicular inflammation, and epididymal cysts than unexposed sons.

New Study Examines DES Daughters Compliance with Breast Screening Guidelines

"Breast Cancer Screening in Women Exposed *In Utero* to Diethylstilbestrol," Elizabeth A. Camp, et al, *Journal of Women's Health*, Volume 18, Number 4, 2009.

Reviewed by Kari Christianson

How much does a woman's understanding of her breast cancer risk affect her compliance with recommended breast screening guidelines? Did DES Daughters follow screening recommendations 15 years ago? Researcher Elizabeth

Camp, MSPH, from the School of Public Health at the University of Texas Health Science Center, and her colleagues with the National Cancer Institute (NCI) DES Follow-up Study examined these questions.

Researchers analyzed responses on a 1994 questionnaire from 3,140 DES-exposed women and 826 unexposed. The women were asked about the number of mammograms, clinical breast examinations (CBE) and breast self-

continued on page 3

els, where numerous urogenital tract abnormalities were observed.

The current paper is unique in that it analyzes all three cohorts of DES exposed sons and looks at the effects of timing and dose of DES. The authors conclude that the lack of effects reported earlier in the Mayo Clinic cohort were due to DES doses being generally lower in this population as compared to the other two cohorts: further the timing of DES exposure varied greatly in the Mayo clinic study. In fact, when dose and timing were considered in the analysis, the magnitude of the association in the Mayo Clinic study was similar to that observed in the overall study.

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DES Action USA

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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

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

The mission of DES Action USA is to identify, educate, support and advocate for DES-exposed individuals as well as educate health care professionals.



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Review of Research on DES Sons from page 1

Thus, the current report confirms that prenatal DES Sons have a higher occurrence of retained testes, testicular inflammation, and epididymal cysts than unexposed sons, and that, similar to DES Daughters, the increased risk is related to timing and dose.

Palmer was particularly interested in the association between prenatal DES exposure and the increased risk for inflammation/infection of the testes. She speculates that some DES Sons, as a result of their exposure, may have been born with a small structural abnormality, such as a minor obstruction, that could explain the greater risk. Palmer calls for follow-up on this point.

Although there are no indications of other urogenital abnormalities, hopefully this combined cohort of DES Sons, who are generally in their mid 50s, will be followed as they age to determine if there is an increased risk of urethral stenosis, benign prostatic hyperplasia (enlargement of the prostate gland), or prostate cancer because those conditions occur more often in older men.

DES Daughter Compliance With Breast Screening Guidelines from page 1

examinations (BSE) they had done in the previous five years.

Camp says the findings show that, "The majority of DES-exposed women receive breast cancer screenings at least at recommended intervals, but over two-thirds do not perform monthly BSEs (breast self-exams)."

"During this study period, there were no specific breast cancer screening recommendations for *in utero* DES-exposed women," Camp clarifies. "Therefore, the recommendations for the unexposed population were applied to all women in this study."

In 1994 at the time of the questionnaire, the American Cancer Society recommended *monthly* BSEs and a CBE (done by a health care provider) every three years in women aged 20 – 39 and annually for women over the age of 40. Mammograms were suggested every year or two for women aged 40 – 49 and annually for women over the age of 50.

"Although the majority of the women in the study were not yet of age for recommended mammography, these data suggest the DES-exposed women (73%) are keeping the recommendation for mammography screening and CBEs (61%), yet the majority failed to perform monthly BSE, with 73% not meeting the recommendation."

In spite of the more recent ques-

tioning of the value of breast self-exams in reducing breast cancer death rates, Camp states that monthly "...BSE remains a simple, cost-free procedure that may detect palpable abnormalities in the breast, leading to earlier professional consultation."

Beyond analyzing the breast cancer screening behaviors of DES Daughters, this study looks at how health care providers can be more proactive in reminding DES Daughters – and all higher risk groups – about recommended screening schedules.

It will be especially interesting to see if knowledge of this increased risk (for breast cancer among DES Daughters) translates into heightened vigilance in doing breast screenings.

There is a need for greater awareness among health care providers about the higher risk of breast cancer for DES Daughters. Camp states, "This DES-exposed population of women will require future efforts to notify them of their increased risk and remind them of the importance of preventative examinations." She suggests possibly utilizing mailed reminders and having doctors promote the benefits of screening exams during office visits.

Additionally, the researchers suggest that access to health insurance,

as well as any health information, may be a factor in the reported screening behaviors and a lack of preventive exams.

This study is important because it sets the mark for researchers to continue reviewing screening behaviors in future questionnaires. The data was developed before it became more widely known that DES Daughters are at increased risk for breast cancer. So it will be especially interesting to see if knowledge of this increased risk translates into heightened vigilance in doing breast screenings.

Camp and her colleagues are currently comparing questionnaire data collected in 2006 with the mammography screening information in this study.

DES Daughters should talk with their health care providers about appropriate breast screening examinations. While access to health care may be an on-going issue, it's vital that DES Daughters — and all women — check their breasts monthly and report changes immediately. It's another way that we can be proactive in our own health care.

Editor's Note:

DES Action USA believes that physicians have a responsibility for any patient with DES exposure history. All health care providers consulted by DES Daughters — primary care, ob/gyns, breast specialists, oncologists — should make efforts, now and in the future, to notify consumers about annual breast and pelvic screenings.

Keeping Track of HRT Study Results

Reviewed by Pat Cody

HRT Raises Ovarian Cancer Risk

"Hormone Therapy and Ovarian Cancer," Lina Steinrud et al, *Journal of the American Medical Association*, 15 July 2009.

In the largest study ever done — over 900,000 women in Denmark aged 50-79 years, during the ten years 1995-2005, researchers studied the connection between postmenopausal hormone treatment and ovarian cancer. Their findings: a 38% greater risk for women on HRT. The conclusion: "Regardless of the duration of use, the formulation, estrogen dose regimen, progestin type, and route of administration, hormone therapy was associated with an increased risk of ovarian cancer."

HRT Linked to Higher Lung Cancer Rates

"Oestrogen plus progestin and lung cancer in postmenopausal women," R.T. Chlebowski et al, *The Lancet*, 20 Sept. 2009.

Our readers will remember that the Women's Health Initiative (WHI) study at 40 U.S. centers was stopped when data showed that risks for heart disease, stroke, thromboembolism and breast cancer rose for those receiving HRT. Researchers, however, have not stopped looking at the data from this project. Now they report a higher incidence of lung cancer in the HRT group, as well as a higher rate of death from lung cancer.

The report was accompanied by this comment from A.P. Ganti M.D. of the University of Nebraska Medical Center:

"Because the optimum safe duration of hormone-replacement therapy in terms of lung-cancer survival is unclear, such therapy should probably be avoided in women at a high risk of developing lung cancer, especially those with a history of smoking. These results, along with the findings showing no protection against coronary heart disease, seriously question whether hormone-replacement therapy has any role in medicine today. It is difficult to presume that the benefits of routine use of such therapy for menopausal symptoms outweigh the increased risks of mortality, especially in the absence of improvement in the quality of life."

Breast Cancer Risk Varies With HRT Dose and Formula

"Estrogen-Progestagen Menopausal Hormone Therapy and Breast Cancer: Does Delay from Menopause Onset to Treatment Initiation Influence Risks?" A. Fournier et al, *Journal of Clinical Oncology*, 14 September 2009.

This French study looked at 1,726 cases of invasive breast cancer among 53,310 postmenopausal women in the 14 years from 1992 – 2005. The researchers noted the types of hormone use, when the treatment began, and how long it was taken. They compared users with non-users (controls) and found a 54% increased risk for women using a combined estrogen/progestagen (synthetic female hormone, called "progestin" in the U.S.) for two years or less within three years of the start of menopause.

However, those using an estrogen/progesterone (natural female hormone) formulation had no increased risk. This is important information for any women considering the use of HRT—both the exact "recipe" of the pills, and the timing.

Age of Puberty Decreasing

Endocrine Disruptors Implicated

Reviewed by Pat Cody

"Recent Decline in Age of Breast Development," Lisa Aksglaede et al, *Pediatrics* May 2009.

This careful Danish study of over 2000 young girls, one group in 1991-93 and a second group in 2006-2008, showed a "significantly earlier breast development in the girls born more recently." The authors noted "alterations in reproductive hormones and body mass index did not explain these marked changes." They found a full year's difference between breast development in the earlier group at 10.99 years and the later group at 9.86 years.

Some researchers believe that

an explanation may be found in the increase of endocrine disruptors in the environment (examples of such disruptors are found on page 5 of VOICE 120 and include such things as bisphenol A which is used in plastics; cigarette smoke; DES, and the herbicide Atrazine).

Tara Parker-Pope, reporting on this study in the May 4, 2009 New York Times, reminds us "early puberty is associated with higher breast cancer risk in adulthood. Early puberty has also been linked with social problems and depression...." She quotes Dr. Aksglaede that "Certainly, it is worrying that we are seeing these marked changes in age of breast development over such a short period of time."

Funding Approved for Important Studies of BPA — A Drug Similar to DES

By Fran Howell

DES researchers were the first to understand how much harm can be caused by prenatal exposure to endocrine disruptors, which are chemicals that interfere with hormone functions. So, when scientists took a close look at the synthetic estrogen bisphenol A (BPA) and recognized the similarities to DES, they paid attention.

BPA was developed at about the same time as DES but is less potent. So DES was given to pregnant women and BPA was shelved until its ability to harden plastics was recognized. Now it is used in the epoxy resins that coat the inside of

food cans, as well as in plastic food storage containers, plastic tableware, water bottles, and even baby bottles. We are exposed to BPA when it leaches into our food and is absorbed by our bodies.

Concerns about BPA regarding health impacts read like those of DES. Infertility, reproductive problems, breast cancer and the threat of problems extending into the next generation are high on the list for BPA studies.

The National Institute of Environmental Health Sciences (NIEHS) has just announced a \$30 million dollar commitment to BPA research over the next two years. NIEHS Director Linda Birn-

baum, Ph.D., says, "Bringing key BPA researchers together at the onset of new funding will maximize the impact of our expanded research effort."

Many of the scientists who now have their BPA studies funded are highly respected DES researchers, too.

Employing the Precautionary Principle, which DES Action USA subscribes to, it may be wise for individuals to limit their BPA exposure now, rather than wait for absolute proof since there is growing evidence of harm. Experts suggest switching to BPA-free water bottles, using glass baby bottles and never using plastic food containers in the microwave.

Beware of Big Pharma!

By Pat Cody

It all comes down to marketing. We keep a close eye on what the drug companies are up to and we've had more than enough to report in recent weeks. Natasha Singer, a writer for the New York Times, described how Wyeth paid ghostwriters for articles in medical journals promoting HRT use. They also paid doctors to sign these articles as authors/ investigators, even though they had nothing to do with the report except allow use of their names. As she wrote on August 19, 2009, "A growing body of evidence suggests that doctors at some of the nation's top medical schools have been attaching their names and lending their reputations to scientific papers that were drafted by ghostwriters working for drug companies — articles that were carefully calibrated to help the manufacturers sell more products."

A month later, Ms. Singer noted, "Some influential medical editors are cracking down on industry-financed ghostwriting. And they are getting help from some members of Congress." Eric

Alterman in the Sept 28, 2009 issue of *The Nation* stated that "in 2008 Harvard earned an F from the American Medical Students Association for its lax conflict-of-interest standards on accepting Big Pharma cash. And back in March, members of its student body... demonstrated against the schools' administration with the intent of 'exposing and curtailing the industry influence in their classrooms and laboratories, as well as in Harvard's 17 affiliated teaching hospitals and institutes." *Dow Jones Market Talk* stated that for January-March 2009, Eli Lilly paid \$22 million to physician 'consultants.'

Why are we not surprised?

Marketing is not limited to payments to physicians. Campaign contributions to Congress led four New Jersey Congressmen to successfully pressure the FDA in 2008 for approval of a controversial patch for knee injuries, despite many studies showing it was unsafe.

We take some comfort in recent federal action to remedy drug company excesses. Pfizer agreed in September to a \$2.3 billion fine to settle both civil and criminal charges that it illegally marketed its (now withdrawn) painkiller Bextra, an anti-psychotic drug Geodon, an antibiotic Zyvox and nerve-pain medicine Lyrica. In 2004, Pfizer was fined \$430 million for illegally marketing an epilepsy drug Neurotonin. Another miscreant, Forest Laboratories, is being investigated by the Senate Special Committee on Aging for its aggressive marketing of Lexapro, an anti-depressant selling for \$87.99 a month compared with \$14.99 monthly for a generic version of Prozac. The New York Times revealed (Sept. 2, 2009) that Forest had plans to send \$34.7 million to pay 2000 psychiatrists and primary care doctors "to deliver 15,000 marketing lectures to their peers in one year."

The more sunshine on such practices, the better we can become as health care consumers. And drug companies are still sponsoring half of the programs doctors attend every year to get their Continuing Medical Education certificates.

DES Action USA works with other organizations advocating for the Physicians Payments Sunshine provision, which is part of the health reform legislation now being considered in Congress.

Major Research Conference Brings Together Scientists and DES Activists

e.hormone 2009: 30th Anniversary Celebration of First Estrogens in the Environment Meeting

By Kari Christianson, DES Action USA Program Director

Something special happened last month in New Orleans. DES activists met with scientists who have labored for years on DES and endocrine disruptor research. They were together for *e.hormone 2009*, a conference hosted by the Center for Bioenvironmental Research (CBR) at Tulane and Xavier Universities.

DES Action USA President Cheryl Roth, Board Member Karen Fernandes, former Board Member Stephanie Kanarek, and I represented the DES community. There was a noticeable energy in the air when we spoke with the renowned scientists and told our DES stories, putting a human face on the issue. These dedicated researchers returned to their labs knowing how vital their studies are to those of us who were exposed to DES.

This mingling of DES-exposed individuals and scientists was unusual because most research conferences entail scientists talking solely with other scientists.

CBR Director, and conference organizer, John McLachlan has been at the forefront of DES research for three decades. Now, as then, DES remains the primary example of how researchers understand the severity of human health effects caused by endocrine disruption.

This year's gathering was billed as an opportunity "to discuss what we know about endocrine disruption, what we still need to know and where it might take us."

The list of speakers and attendees is a "Who's Who" of endocrine disruption researchers. Many have devoted their careers to understanding how DES and other endocrine disruptors, such as BPA, pesticides and herbicides, affect the environment and health into future generations.

DES issues were a priority, with one session devoted entirely to DES research findings. Six separate topics or areas of research were highlighted in: *The DES Experience – A Model for Environmental Endocrine Disruption and Transgenerational Disease.*

- Retha Newbold from the National Institute of Environmental Health Sciences spoke on "Developmental Exposure to DES" and her research using the mouse model.
- Cheryl Walker from the University of Texas M. D. Anderson Cancer Center presented her study "Gene Imprinting with DES in rats," about developmental reprogramming as the fetal basis of adult disease.
- Linda Titus-Ernstoff of Dartmouth and a Principal Investigator spoke about the "Recent Results with DES-

Exposed Humans." She offered a complete summary of the current findings of the National Cancer Institute DES Follow-up Study, including her work focusing on DES Grandchildren.

- Doug Ruden of Wayne State University spoke about "Epigenetics, Estrogen, and Development."
- Lindsey Berkson, author, nutritionist and DES Daughter, addressed the "Personal Experiences and Speculation in DES Exposure."
- DES Action USA representatives shared our personal health stories, reproductive histories, family experiences, as well as our needs and hopes for more human generational research, during the segment titled, "Lessons Learned."

The Anniversary Gala banquet recognized four individuals for their contributions to research and for sounding the earliest warning sirens that use of estrogenic compounds would have lasting adverse effects. These individuals tenaciously voiced their concerns at a time when few other researchers, medical professionals or government institutions paid heed. Honored were researchers Howard Bern, Theo Colborn, Roy Hertz and DES Action Co-Founder Pat Cody.

These annual e.hormone Conferences establish a "think tank," with attendees sharing ideas and building relationships for future research. The scientists are energized about pursuing their DES work and understanding the concerns of those who were exposed to the drug.



"Guardians of the Galaxy" Gathering
Left to right: DES Action's Christianson, researchers McLachlan, and Titus-Ernstoff,
DES Action's Kanarek, researcher Newbold, and DES Action's Roth and Fernandes

Intriguing New Book Describes the Health Movement That Is The DES Experience

Reviewed by Christine Cosgrove

DES Action USA member and coauthor of Normal at any Cost: Tall Girls, Short Boys, and the Medical Industry's Quest to Manipulate Height.

Susan Bell, a professor of social sciences at Bowdoin College, brings a feminist scholar's sensibility to the stories of 20 women whose lives were disrupted by cancer, miscarriage, and infertility due to their exposure to DES. In her book, DES Daughters: Embodied Knowledge and the Transformation of Women's Health Politics (Temple University Press, 2009), Bell argues that feminism, the fledgling women's health movement, and the discovery that DES caused cancer and reproductive abnormalities in children of women prescribed it during pregnancy combined to produce what social scientists call an "embodied health movement."

These movements arise from an illness or medical condition, such as AIDS or breast cancer, and typically challenge existing medical/scientific knowledge and practice. They are also characterized by the involvement of activists and the formation of organizations, such as DES Action and DES Cancer Network, which eventually lead to collaboration with scientists and health professionals in pursuing treatment and expanding research funding.

Bell suggests that in the years since the connection between DES exposure and clear cell cancer was discovered in 1971, the DES experience evolved into an embodied health movement.

Her evidence is based on the personal stories of DES Daughters she interviewed. The recorded interviews were transcribed verbatim. Bell parses each woman's sentences, looking for clues to how each feels about her DES exposure, the information she received from her doctor, the way she received that information, and her reactions to it.

Bell describes how these women react differently as knowledge and attitudes

about health and the roles of doctors and patients gradually changed.

Esther, for example, was 22 when diagnosed with vaginal cancer several years before the DES link to cancer was made. Her surgeon told her she needed a hysterectomy and he might have "to take more things out."

Bell suggests that Esther was left in the dark about what was happening to her body. Her surgeon operated, removing her vagina, bladder, urethra, uterus, right ovary and fallopian tube in a "heroic" attempt to save her life. Heroism in medicine was what was expected back then.

Fast forward to 1981 when Molly finds a lump while inserting her diaphragm. At almost 26, she had earlier read *Our Bodies, Ourselves* and later, after learning she might be a DES Daughter she located a clinic with DES-experienced physicians. Although told she was past the age of clear cell cancer, she knew enough to be suspicious when she felt the lump.

When Molly disagreed with the pro-

posed course of treatment she was selfconfidant enough in her own knowledge of her body and DES to seek out another doctor.

The stories these two women tell, and those of the others in the book, show how much has changed in a relatively short time.

For the casual reader, some of the scholarly terminology can be daunting. (If you're not up on Foucault and his theories, a quick check on Wikipedia can help.) But there is plenty in this book for non-academics. The narratives are moving, and Bell's view of how individually and collectively DES Daughters created an embodied health movement is intriguing.

Temple University Press has generously offered DES Action USA members a 20% discount when they purchase this book. Use promo code TDESA09 at www.temple.edu/tempress or by calling 1-800-621-2736. The discount is good through the end of December.

Eli Lilly Can't Have It Both Ways

There's something deeply disturbing about a company manufacturing products that cause cancer, as well as drugs to treat cancer.

That's what pharmaceutical giant Eli Lilly is doing as the sole worldwide producer of rBGH (recombinant bovine growth hormone). Injected into cows to make them lactate longer and produce more milk, rBGH contains elevated levels of a protein known to increase breast cancer risks.

Last year DES Action USA joined Breast Cancer Action in pressuring General Mills to stop making Yoplait yogurt from milk containing rBGH. Dannon followed suit shortly thereafter.

Corporations like Kroger, Walmart and Starbucks already refuse to sell milk



tainted with rBGH. It is time to stop production all together and eliminate rBGH from our food supply.

Those of us in the DES community know Eli Lilly as the largest producer of DES. We didn't understand its danger at the height of its use. Now that we have concerns about rBGH we won't stand idly by.

You can help us pressure Eli Lilly to get out of the rBGH business by sending them an email. Go to www.milkingcancer.org and do so today.



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