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A Focus On Diethylstilbestrol

SPRING 2013 #136

Additional Health Problems Possibly Linked to DES

Associations found in both DES Daughters and DES Sons

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

Reviewed by Fran Howell

Analysis of health information from DES Daughters and DES Sons found a higher incidence of diabetes, cardiovascular disease, coronary artery disease, heart attack, high cholesterol, hypertension, osteoporosis and bone fractures, which may be associated with prenatal DES exposure. The new findings were published in the journal *Epidemiology* by researchers with the National Cancer Institute DES Follow-up Study.

Participants in the Study complete questionnaires on a five-year cycle. Information was taken from responses to the 2001 and 2006 surveys provid-

ed by 5,590 women and 2,657 men in matched cohorts of DES-exposed and unexposed individuals. All have medical record confirmation of prenatal DES exposure, or non-exposure.

The questionnaires asked participants if they had been diagnosed with any "serious medical conditions that required hospitalization, surgery or long-term treatment." Those who answered in the affirmative were then provided

a list of specific conditions: adult-onset diabetes, high cholesterol, hypertension, coronary artery disease, myocardial infarction (MI; heart attack), stroke, osteoporosis, and fractures. For analysis the categories of stroke, coronary artery disease and MI were combined to create the cardiovascular disease (CVD) category.

An open-ended question for re-

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Higher incidence percentage in women and men prenatally exposed to DES, compared to those not exposed, for the following conditions:

Condition	DES-Exposed
Diabetes	21%
High Cholesterol	12%*
Hypertension	14%*
Coronary Artery Disease	18%
Myocardial Infarction	28%
Stroke	55%
All CVD	27%*
Osteoporosis	24%
Fractures	30%

**Difference between exposed and unexposed is statistically significant (i.e., unlikely to be due to chance) but doesn't prove DES was causal.*

Thirty-Five Years of Action— We Thank Amazing Individuals

By Kari Christianson

Where would we be without the founders of DES Action USA? These tenacious mothers, daughters and health activists knew something was wrong and demanded answers about DES.

DES Mothers asked how a drug they were given to prevent miscarriage or that was mixed in prenatal vitamins could have harmed their children? They wanted to know what they could tell their daughters and

sons about their future health. Who was responsible for this tragedy?

There were no easy answers, but these DES Mothers didn't give up.

Then DES Daughters, informed health professionals and activists joined in demanding answers. DES Sons added their voices a few years later.

The first flickering of a movement occurred nearly simultaneously all across the country. In such far flung places as California, Connecticut,

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DES Action USA
P.O. Box 7296
Jupiter, FL 33468

info@desaction.org
www.desaction.org

Yes!—I want to join DES Action to stay informed and support a cause I believe in.

All members receive **The DES Action Voice** quarterly. Those at the **\$100 level and above receive an annual report on DES Action's work and progress.** All contributions are **tax deductible.**

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Please make checks payable to **DES Action.**

I am a: ☐ DES Daughter ☐ DES Son ☐ Other ☐ DES Granddaughter or Grandson
☐ DES Mother of a: ☐ Daughter ☐ Son

NAME

ADDRESS

CITY | STATE | ZIP

PHONE

E-MAIL ADDRESS

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 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

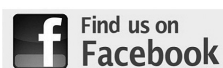
You'll receive an e-mail back from Yahoo! Groups confirming your request to join. It offers two registration options and the easiest is Option 2. Click "Reply" so the note is sent back.

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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Contacts

United States

DES Action USA Headquarters

P.O. Box 7296
Jupiter, FL 33468
info@desaction.org
www.desaction.org
800-337-9288

DES Action Related Organizations

Australia

DES Action Australia, Inc.

PO Box 282
Camberwell 3124 Vic. Australia
info@desaction.org.au
www.desaction.org.au

DES Action Australia - NSW

14 Edmundson Close
Thornleigh NSW, 2120
Australia
C_devine@bigpond.net.au
www.desnsw.blogspot.com

France

Reseau DES France

12 rue Martinon
40000 Mont de Marsan
France
reseaudesfrance@wanadoo.fr

The Netherlands DES Centrum

Wilhilminapark 25
3581 NE Utrecht
The Netherlands
des@descentrum.nl
www.descentrum.nl

MISSION STATEMENT

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1- (800) DES-9288 (800) 337-9288

info@desaction.org

www.desaction.org

Executive Director

Fran Howell

Program Director

Kari Christianson

Board of Directors

President: Jill Vansalous Murphy

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Linda Marks

Litsa Varonis

Jackie White

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Additional Health Problems

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porting additional information relating to other unlisted conditions was included on the forms, also.

Researchers took into account additional risk factors for the medical conditions being studied. They found, “Exposed women were younger, had more years of education, and were less likely to smoke than the unexposed, but the two groups were similar in body mass index (a measure of fatness) and alcohol intake. Frequency of general physical examinations in the past five years was slightly lower in the exposed women. Exposed and unexposed men were similar to each other in demographic and lifestyle characteristics.”

Also, according to maternal pregnancy history for the group of DES Daughters and Sons who developed diabetes or high blood pressure, none of their mothers were prescribed DES for those particular medical conditions.

The researchers found associations between DES and the health issues under study, “generally were weaker in

the men compared with the women,” although they noted the incidence of stroke and osteoporosis turned up higher in exposed than unexposed men.

While the condition of cardiovascular disease and its risk factors such as hypertension and high cholesterol, along with diabetes and osteoporosis appear greater in DES Sons and Daughters than in the unexposed cohort, only a few of the associations could not be explained by the role of chance, including high cholesterol, hypertension and all cardiovascular disease. The increase in incidence did not differ by the DES exposure. For several other health outcomes related to DES, not part of this study, dose and timing do matter.

Big Picture Understanding

Both nationally and internationally, researchers are studying the role that endocrine disruptors may play in human health, particularly regarding cardiovascular disease. So this study, which suggests an association between DES and CVD, is important. And, as is

often the case in DES and all research, additional study is needed. In particular, it will be important to verify the details of the disease and its diagnosis.

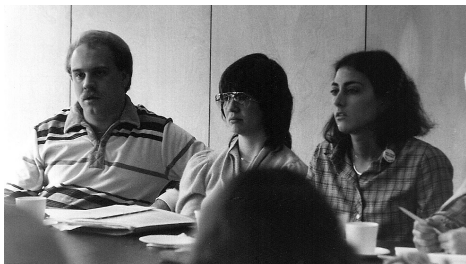
Scientists have begun to see mounting evidence that indicates concentrations of persistent organic pollutants, like dioxin, DDT and PCBs, in humans may be linked to increased risks for diabetes and cardiovascular diseases. Therefore, this research finding regarding the endocrine disruptor DES and its association with those health issues is telling. It’s the first study associating DES exposure with these adverse health effects.

The connections made between prenatal DES exposure and adult onset of disease will keep the matter in front of researchers working to unravel the mysteries of how prenatal environmental exposures affect human health.

Scientists on this study say they plan to continue following the health of participants, both DES-exposed and unexposed, as they age into the time when diabetes, and cardiovascular disease and its risk factors become more prevalent.

Amazing Individuals

continued from page 1



Illinois, Massachusetts, Washington, DC, Maryland, New Jersey, Pennsylvania and New York, individuals came together—bringing their questions about current and future adverse health effects to hospitals and health clinics, which in turn provided space for meetings.

Compelling newspaper articles helped spread the word that DES grassroots groups existed in several states, causing public interest in DES exposure to grow. In 1977 the activists, who wouldn’t take “no” for an answer, met one another face-to-face for the first time and vowed to stay in touch to work together. They were

good to their word even though it wasn’t easy.

The computers, email, websites and cell phones with unlimited minutes that we take for granted today didn’t exist back then. Using what now seems like primitive technology, they communicated DES information loud and clear. Nothing could stop these determined individuals, who, in 1978, came together to incorporate DES Action as a national organization to address the needs of the DES-exposed.

These dedicated individuals spoke truth to power—demanding answers from elected and appointed leaders. They traveled to Washington, DC, to tell government officials that DES was an important health issue in serious need of research funding. They worked together on the state and



national level to enact legislation for education campaigns and to prevent insurance discrimination. And they reached out to find more DES Mothers, Daughters and Sons. There were disappointments along the way, but their successes started stacking up.

The title of DES Action Co-Founder Pat Cody’s 2008 book says it all—*DES Voices: From Anger to Action*. Angry mothers, guilty mothers, brave daughters, scared daughters, questioning sons and concerned health care providers all came together to make sure the DES health issue was not ignored. And it most certainly would have been ignored had they not organized.

We look back with pride at those who gave DES Action such a good start. It’s their actions and their voices, along with ours, that live on 35 years later.



What Happens in the Lab Should Not Stay in the Lab

Making Scientific Research Findings Available to Doctors

It seems obvious that research results should drive health care for those exposed to DES. But there's long been a disconnect between knowledge generated in research laboratories or cohort studies and what doctors know about the impacts of DES exposure.

It isn't just a DES problem. Sadly, life-saving information often doesn't travel from the world of research into the realm of medical practice. Attendees to the Women's Environmental Reproductive Health Consortium want better collaboration between scientists and doctors.

Hosted by the National Institute of Environmental Health Sciences (NIEHS), researchers shared updates to help scientists working on the same issues, but laboring separately in their own labs. Time and time again it was made

clear that looking for and understanding environmental exposures during pregnancy has the potential for improving the health of mothers and their children. Jeanne Conry, M.D., Ph.D., president-elect of the American College of Obstetricians and Gynecologists, wants to move quickly to translate scientific knowledge into prenatal care clinical practice.

One suggestion is to present study results during large medical profession conferences. Research given to doctors this way might be incorporated quickly into patient care. It also allows scientists to meet the end-users of their data to move their findings from the laboratory bench to bedside.

National Toxicology Program lead researcher Suzanne Fenton,

Ph.D., brought the conversation around to DES when she described an important new study to identify a metabolic fingerprint, or biomarker, for prenatal DES exposure!

While useful to researchers who need proof of exposure to properly study the effects of endocrine disruption, this knowledge could someday be used to test individuals for DES exposure. What an exciting example of translating research into real world use! You'll read more about the search for a DES biomarker in a future issue of the DES Action VOICE newsletter. **DES VOICE**



Suzanne Fenton describes her new study to identify a fingerprint, or biomarker, for DES exposure.

DES Health History Questionnaire Now Being Tabulated

Analysis of the DES Action Health History Survey continues!

Deborah Wingard, Ph.D., an epidemiologist and Professor in the Department of Family & Preventive Medicine at the University of California San Diego, has collected and is analyzing responses to the 2012 DES Action questionnaire.

These responses are being compared with national health information incidence gathered by the Centers for Disease Control and Prevention. It's a detailed process that requires patience, as well as expertise.

DES Action members will have access to the results when they are finalized and published in an upcoming issue of the VOICE later this year.

Prenatal DES Exposure Linked to Early Menstruation May Have Ties with Breast Cancer Risk

"Prenatal and infant exposures and age at menarche," Aimee A. D'Aloisio et al., *Epidemiology*, 2013 March; 24(2): 277-284.

Reviewed by Kari Christianson

Early menarche (the first menstrual period) is identified as an increased risk factor for breast cancer. So researchers with the National Institute of Environmental Health Sciences Sister Study, who are following the health of over 50,000 sisters of women with breast cancer, asked about the age of a first period to identify any common factors in early menarche.

DES was found to be one of the prenatal exposures most strongly associated with very early menarche (at or before age 10). Other factors associated with very early menarche were maternal pre-pregnancy diabetes and pregnancy-related hypertensive disorder. Soy formula was associated with both very early menarche and late menarche.

The researchers also found that DES was associated with early menarche (at or before age 10 or 11). Other factors associated with early menstruation are low birth weight, having a teenage mother, being firstborn, as well as maternal smoking, pre-pregnancy diabetes and pregnancy-related hypertensive disorder.

Sisters of women who have had breast cancer allow researchers to study shared genes and environment, which may help identify risk factors and lead to ways for preventing breast cancer.

Corroborating this study, research done by the National Cancer Institute DES Follow-up Study also has reported an association between DES exposure and very early menarche.

As researchers from the Sister Study state, "Our study adds to prior evidence that early-life exposures influence age at menarche Greater understanding of the possible biologic mechanisms that could explain our findings is also an important area for future research."

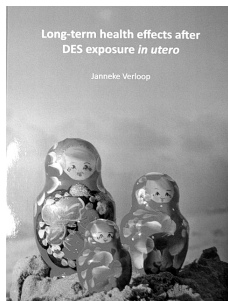
DES VOICE

"DES Effects: What More to Expect?"

INTERNATIONAL RESEARCH SYMPOSIUM IN AMSTERDAM

By Kari Christianson

Our colleagues at DES Centrum in The Netherlands hosted a daylong symposium with speakers from the U.S. and The Netherlands. The occasion was the doctoral defense panel for Janneke Verloop, a researcher who has been instrumental in analyzing responses of DES-net, a study of over 17,000 suspected and known DES-exposed women and men in The Netherlands. On her thesis cover are nesting dolls, which represent the reality and potential of continuing harm caused by DES.



ed health problems via Skype. He is an early pioneer in the study of estrogenic effects on fetal development and on environmental endocrine disruption,

Three Dutch researchers presented new findings from their DES-net studies, some of it focusing on DES Sons and Grandsons. Because these studies are embargoed, we await publication before providing a review.

One of the vexing questions tackled by a panel of international researchers and clinicians is the development of screening recommendations for DES Daughters as they age. Variations exist between countries, and there are questions about how to evaluate current practices.

Participants at the "What more to expect?" symposium acknowledged



Top Row: Matti Rookus, The Netherlands researcher; Janneke Verloop, The Netherlands researcher; Maria Zwart, DES Centrum; Anne Levadou, DES Reseau. **Bottom Row:** Kim Karsenberg, DES Centrum; Elizabeth Hatch, USA researcher; Kari Christianson, DES Action USA; Pamela Solere, DES Reseau (France).

that additional research is needed into the DES breast cancer risk, as well as additional study of DES Sons and DES Grandchildren. Joint analysis of data from different countries would be very helpful.

DES VOICE

One 2010 study from Verloop's DES-net work found no increased incidence of breast cancer in Dutch DES Daughters. But, as pointed out during the symposium, the total dosage of DES given during pregnancy in The Netherlands was lower than in most parts of the U.S. This difference may account for varied study results reported in different countries.

Long-time DES researcher with the National Cancer Institute (NCI) DES Follow-up Study, Elizabeth Hatch, Ph.D., provided a complete overview of U.S. findings in the NCI study. These include the mechanism by which DES causes harm during prenatal development, altering tissue and function, as well as questions about how DES affects future generations.



Researcher Elizabeth Hatch gives an overview of U.S. studies.

John McLachlan, Ph.D., Tulane University and previously Scientific Director at the National Institute of Environmental Health Sciences (NIEHS), offered more insight into biological mechanisms of DES-relat-

Reflections On Strengthening International Connections

By Kari Christianson

DES research conferences are few and far between, so being invited to one in Amsterdam was a true opportunity. I was able to spend quality time with both DES researchers and activists from The Netherlands and France. As Program Director of DES Action USA, it was an honor to make the trip.

What a day it was! Following the symposium I was delighted to witness Janneke Verloop present her doctoral thesis and defense to a panel of scholars. She did an outstanding job in front of a large audience, with a panel of scholars ultimately rewarding Verloop with her Ph.D. in epidemiology during a dignified and poignant ceremony!

The next day, three researchers and DES leaders from The Netherlands, France and USA held our own meeting. It's rare we can meet

face to face like this. We discussed the challenges of funding for combined projects among international countries, as we all look for new DES insights.

Perhaps most of all, spending time with other DES Daughters and Mothers was a real treat. In sharing our DES stories we saw how remarkably similar they are, no matter where we live. Connecting with the researchers added to our bond, as they are so committed to getting answers about DES. It fuels our resolve to keep DES voices strong.

I am grateful to DES Centrum for organizing the event that allowed for important connections to be made that would not have happened otherwise. I'm thankful for the kindness and attention to detail by Maria, Kim and everyone with DES Centrum, who made my time in Amsterdam very special and productive!

DES VOICE

LETTER TO THE EDITOR

Immune Dysfunction a Concern

Mono-nucleosis was something I knew all too well. Endured it at age 16 and was diagnosed again at age 23. A year later—mono and titer changes again.



Sarah Sommers

Got better with rest, but another year and the same diagnosis, with additional problems, including postural orthostatic tachycardia, headaches, nausea, weight loss (20 lbs. to the point people started wondering if I had leukemia).

Dr. Wesley Fowler, at the University of North Carolina, has done research with Dr. Arthur Herbst and had followed me for DES exposure since I was nineteen. He connected me with a physician in immunology, and all agreed my immune system was not working correctly. Documented.

Later, vertigo began and diarrhea, which led to hospitalizations and C. Difficile GI infection in the absence of antibiotics, which is unusual. It was a difficult and dangerous year until I could be stabilized.

My husband and I then decided to start our family. Knowing what we do about DES, I was surprised—in a good way—when I became pregnant. Around the 14th week, cervical thinning and dilating started and frightened my obstetrician, who had been sure all would be “just fine.” A cervical cerclage was performed and I went on strict bed rest. My mother raised concerns about travel, so in a first for my doctor, he sent his nurse for weekly visits to see me at home. I credit mom for speaking up! To our joy, our son was born, six weeks early, but he was OK.

Within a year I developed another episode of mono, then other problems. Natural Killer cells were normal in number but not in function; cytokine

levels skyrocketed, cardiac dysfunction worsened and recurrent C. Difficile illness, CDAD, returned. I still contend with it all today.

But worse yet, when our son was five, he had constant strep throat infections. Then at age seven, full blown mono with mycoplasma pneumonia. As he grew (or didn't very well), he had other mono episodes and pneumonias. He had/has asthma and fell off the growth chart, looking three years behind his true age. He, too, was diagnosed as having immune system problems with concerns regarding endocrine function.

My son DID grow, and, as his testosterone kicked in, it seemed he was healthier. But he did have prostatitis episodes that began in college in the absence of any STDs.

I remain concerned for his health, as well as for any offspring, when, and if, he decides to have a child. Effects remain unknown regarding DES Great-Grandchildren, especially in the areas of immune and endocrine functioning.

I've had horrible periods, abnormal Pap smears, biopsies and a high-risk pregnancy. None of that compares to my struggle with immune system dysfunction.

This is why I strongly ask you to tell researchers not to look for a “disease”—look for messed up immune systems! Animal studies have shown immune abnormalities, but not specific “diseases.” When I asked Dr. Fowler what immune dysfunction looks like in DES Daughters, his response was: “Very similar to what I see in you.”

Mouse studies showed immune problems, but human DES studies have yet to show “immune system diseases.” Why are researchers looking for known diseases at all? Are the studies adequate? I don't think so. Are they asking the right questions? I don't think so.

The sheer number of pregnant women given DES and the sharp rise in unusual immune system problems in this country doesn't seem coin-

cidental and shouldn't be ignored. While I have coped, my immune system issues are debilitating. Other DES Daughters and DES Sons have similar experiences and their voices deserve to be heard and heeded with appropriately strong research.

Science can do better by us, our children and future generations. We don't know what faces DES Grandchildren and Great-Grandchildren regarding immune/endocrine dysfunction. I didn't say “diseases.” We KNOW immune system dysfunction in many exists. Timing and dose DOES matter and the researchers know it from animal studies. They need to rigorously and wisely pursue investigations using smart science.

Sincerely,

Sarah Sommers

(DES Grandson granted use of his information)

EDITOR'S NOTE:

Many factors, which may or may not be associated by prenatal DES exposure, may be involved in the development of any health issue. The fact that not all DES-exposed individuals have the same health or reproductive health issues is the challenge that researchers face on a daily basis. And, while the mouse model has been of remarkable help in understanding the health consequences of DES exposure, we must remember that these mice are housed in the same environment and exposed in a consistent manner, according to the study protocol. Mouse models are helpful but may not reveal the whole story for humans. The health experiences cited in this Letter to the Editor and the challenges raised by the author provide an important perspective for our members and, hopefully, for researchers.

How did she get it so right?

The Author Of A DES Novel Is Not DES-Exposed!



Judith Barrow's book, *Silent Trauma*, was published earlier this year and is garnering excellent reviews. We wanted to know more about the author, who lives in Pem-

brokeshire, Wales, to find out how she came to write this compelling novel.

DES Action: Is it true you are not DES-exposed?

Barrow: I was not personally affected by DES and was lucky enough to have three children, a girl and then twins. But I did have 'odd' cells when I was 32 that resulted in a hysterectomy. Then 15 years ago, I was diagnosed with breast cancer. So, I've experienced medical problems known well by many DES Daughters.

DES Action: What led you to write a book about DES?

Barrow: Some of my relatives had health issues, but they didn't know why. When I heard a radio interview about DES, things fell into place. We talked and realized they had been exposed to DES. But they're private people who felt more comfortable having me look into it. So I did, and found DES Action UK. I learned so much about being exposed that, when I was asked by DES Action UK to write an article about it, I was happy to help. After that I received numerous letters from DES Mothers and Daughters. You can see how that experience translates into the plot line when you read my book.

DES Action: It sounds like you were drawn into the issue.

Barrow: Oh yes. I joined members of the DES group in writing to lawmakers, government health officials and celebrities about DES, to no avail. It was eye-opening. I truly felt the frus-

tration and pain, and was determined to spread awareness about DES.

DES Action: When did you decide to write a book?

Barrow: It was 1996 when I started thinking about using my writing skills for the cause. I'm a writer, after all, and figured maybe I could craft a story that would be widely read about what happened to those exposed to DES. It took quite a bit of research, but that's something I thrive on. Once I collected all of my notes, I knew I could write a story that could reach people. So *Silent Trauma* evolved.

DES Action: But 1996 was a long time ago.

Barrow: True enough. But I'm a meticulous researcher and had a lot to learn. And I never forgot for a moment that I was writing about a serious fact of life for many. Once I was comfortable in my understanding of DES exposure and the emotions it generates, it took about three years to craft the story and weave four lives into it. I wanted to get the balance right and still make my novel a good read.

DES Action: *Silent Trauma* is remarkable in how well it sticks to historical facts and the harm caused by DES.

Barrow: It's definitely a work of fiction based on fact. Research is extremely important to me, so I spent a considerable amount of time checking and rechecking facts to get them right.

DES Action: We repeatedly hear that you nailed the emotional responses of DES Daughters and Mothers. Many say they saw themselves in your characters.

Barrow: I'm pleased to hear that and it means a lot. Of course, I went through some emotional health issues myself. But it was communicating with members of DES Action UK that helped me really understand. And, of

course, I'm a mother, so I could see the tragedy through those eyes, too.

DES Action: How did you create your characters with such authenticity that readers forget they aren't real?

Barrow: I figure out their personalities first, then spend time getting to know them. What they look like, where they live and how they react in different situations are all important. How do they deal with conflict in their lives? No one is one-dimensional, neither good nor bad, so the women I wrote about aren't either. I get a picture in my head of who they are so I can tell their stories. It's interesting that what I had in mind at the beginning isn't how the book turned out. The characters actually led the way and changed the story as we went along. They are all strong women.

DES Action: And you had to be strong to get *Silent Trauma* into print.

Barrow: I guess I shouldn't have been surprised, but I was. My publishers wouldn't take it, and when I went to various others, I got the same responses. They told me they "could be sued because DES effects have not been proven in the UK," while the other reason for rejecting it was because, "no one wants to read an issue-led novel." So I published it myself, and I'm proving them wrong!

DES Action: Dreaming a bit—have you thought of who should play the parts if a movie is ever made of your book?

Barrow: I see Judy Dench as Meg, Gaynor Faye as Jackie, Natalie Portman as Rachel, Cate Blanchett as Avril (but she'd have to put on a few pounds!).

Silent Trauma is available in paperback and in Kindle format at: www.amazon.com

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Victory Turns to Dismay in Boston DES Breast Cancer Litigation; New Lawsuits Filed

When Eli Lilly offered a settlement that abruptly ended the first DES breast cancer trial in January, it was anticipated subsequent settlement offers would be made to other DES Daughters whose breast cancer cases are pending.

But, unfortunately, that was the last offer Lilly has made.

Attorneys Aaron Levine and Julie Oliver-Zhang are moving forward on two fronts. They've asked Boston U.S. Magistrate Judge Marianne Bowler to consolidate four cases, so they can be tried together this summer. And they've filed two new DES breast cancer cases in Washington, D.C.

The D.C. judge has been asked to expedite the trials, and a decision is pending. Oliver-Zhang says these two can be considered bellweather



cases, meaning they are representative of the plaintiff pool. When tried, they will give an indication of the strength of DES breast cancer cases as a whole. Once a settlement or a verdict is reached, the value should serve as a guideline for the resolution of other DES breast cancer lawsuits.

According to Oliver-Zhang, one

of the plaintiffs in the D.C. litigation has a particularly heartbreaking story. She suffered an incompetent cervix that led to the premature birth of her daughter, who suffers from cerebral palsy as a result. Wheelchair bound, she needs round-the-clock care with her mother being the primary caretaker. Then at age 52, this DES Daughter received a devastating diagnosis—Stage III breast cancer.

As for the plaintiffs in Boston, all four are from New York State and Oliver-Zhang describes them as committed and enthusiastic about taking their cases to a verdict.

You can count on DES Action USA to keep you informed of this important litigation via the VOICE newsletter, on our Facebook page, and, coming soon, through email alerts.

DES VOICE