A FOCUS ON DIETHYLSTILBESTROL

Summer 1991

#49

# Still With Us:

## Research Needs of the DES-Exposed

estimony by Board Member
Margaret Lee Braun, Director of the DES Cancer
Network, to the Office of Research
on Women's Health, National
Institutes of Health, June 12. The
Cancer Network, an affiliate of DES
Action, provides support and
medical information for women who
have had clear-cell cancer.

1991 is the 20th anniversary of the link between clear-cell cancer of the vagina and in utero exposure to diethylstilbestrol (DES). That discovery was the beginning of a story that is still unfolding: the story of DES research.

In 1971 doctors at the Massachusetts General Hospital saw eight young women with an extremely rare form of invasive vaginal cancer. The cancer had only rarely occurred in medical history, and never in women so

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young. The patients' ages ranged from 14 to 22 years. They had one thing in common: their mothers had been prescribed the drug DES during pregnancy. This powerful synthetic estrogen was given to five million American women over a 30 year period, between 1941 and 1971, in the mistaken belief that it would prevent miscarriage.

In fact, the drug was untested for pregnancy use. And although it was known in the scientific literature as early as 1939 that DES caused uterine cancer in laboratory animals, and although it was known as early as 1953 that DES had no beneficial effect whatsoever on miscarriage, DES was aggressively marketed until 1971—when the link to cancer was established.

1971 was an important year for me also. I was 19 years old. That fall I lay in a hospital bed in Boston in excruciating pain. A young doctor, dressed in a dark suit and tie, sat uncomfortably on the edge of my bed. He told me that he was going to have to remove my uterus, fallopian tubes, ovaries, lymph glands, vagina and bladder—in order to save my life—because of a drug prescribed to my mother almost 20 years before.

I survived clear-cell cancer, but I, and 10 million other DES-exposed people, do not know what lies ahead for us.

### Research Needs

Although the majority of DESexposed are still in their 30s, DES research has dwindled to practically nothing. We do know that DES crossed the placenta and damaged the reproductive system of the developing fetus, but the full range of reproductive injuries, and injuries to other body systems (endocrine, immune and cardiovascular) have not been identified because no inclusive studies of the population are underway.

There do exist major DES studies that have assembled large cohorts over long periods. Yet these three cornerstone studies are hanging by a thread. The DESAD Project, which for 15 years has followed 3300 DES daughters at five different medical centers, was denied funding in 1990. At the last minute the

continued on page 6

### **Get Into Action**

DES Action USA could not have originated and grown without the dedicated efforts of volunteers. Today, we proudly boast the activities of over forty DES Action groups across the country and around the world. The foundation of each group was created and nurtured by volunteers. We still need you. Write your group today. Offer your services for a few hours a week. Become a part of the action with DES Action.

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### 37 "New" Women Contact the DES Cancer Network

Retwork (DCN), with the help of Dr. Arthur
Herbst, sent a letter to all clear-cell cancer survivors listed in the Herbst Registry So far, 37 cancer daughters who have never been in touch with the DCN before have contacted Margaret Braun, the Director of the DCN. Margaret has written to all of these women, and members of the Network are calling each of them.

If you or anyone you know (attorneys, gynecologists, nurses, etc.) knows a clear-cell cancer survivor who has never been in touch with the DCN, please tell them to write: The DES Cancer Network, Box 10185, Rochester, N.Y. 14610. The goal of the DCN is to reach out to all clear-cell cancer survivors, to widen the circle of the DCN, and to make a difference in each survivor's life.

So far, about 200 women who had clear-cell cancer are members of the DCN. Some women contact the DCN from five-to-ten years after their cancer, although many newly diagnosed patients get in touch sooner. The DCN is a support network, provides medical and legal referrals, and works to influence researchers to find answers to so many unanswered questions about clear-cell cancer.

The DCN needs your help to locate all of the DES clear-cell cancer survivors. You can also reach Margaret at (716) 473-6119.

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### **Notes from Nora**

relcome to Notes From Nora, a new column which will regularly appear in the Voice. This column will allow me to share my thoughts and plans with you as our Board and I work to lead DES Action forward through the 1990s. I would also like you to use this space, so please write your comments, questions, and ideas to me, especially if you have thoughts which may not fit in our traditional "Dear Doctor" or "Letters" sections (such as a great fundraising tip or an organizing strategy, or just a concern on your mind).)

On my mind this summer is our campaign to convince Congress and the National Institutes of Health (NIH) to allocate significant funds for DES research. You may have noticed that we're talking about research quite a bit these days, from these pages to our last two fundraising appeal letters. That's because there is finally awareness on Capitol Hill about the vast inequities in funding for "men's" and "women's" health issues, and thus a window of opportunity for us to seek attention to what has traditionally been seen as primarily a women's health issue. In reality, DES affects women and men, who together cope with the effects of DES on themselves and their wives, sisters, or daughters. We seek studies on DES sons at the same time that we lobby for research on mothers and daughters.

In this issue you'll read our testimony as it was presented to the NIH Task Force on Opportunities for Research in Women's Health. The testimony was very well received and made a significant impression on the Task Force. While in Washington our representative, Margaret Lee Braun (board member and Director of the DES Cancer Network) met with members of Congress, women's health organizations, and officials in the National Cancer Institute and NIH. We join with organizations for survivors of breast cancer, ovarian cancer, and other groups in waging an uphill battle for funding in a time of cutbacks and "austerity" for social services.

Convincing the government to make DES research enough of a priority to allocate sufficient funds for long-term, sizeable human studies (such as the DESAD study) will not be a quick or easy task. But I believe that we can do it.

Lately I've been thinking about the loose-knit DES network which exists among all of you reading this newsletter. We have a community of DES mothers, daughters, and sons across the United States whose great diversity is our weakness and our strength. We come from many walks of life and span a great range of differences. Most of us are strangers to one another. Yet by virtue of our common concern about DES we encompass a wealth of knowledge, experience and social strata. We are in every great city and small rural town. And if we only begin to talk to our neighbors, friends, and coworkers, we can make this fragile network a true community of support and action. To bring about our goal of research, we will need the involvement of all of our members and more. We will need support from everyone exposed to DES, their families and friends. You may be surprised to learn that someone you work with every day is also a DES daughter, son, or mother. We need them to join DES Action and to be ready to spring into action as our research campaign unfolds. We need them to make this a community with power.

### Study of Chicago Group

new study on the health histories of about 275 DES daughters and a similar number of DES sons is underway. The University of Chicago is collaborating with the National Institute of Environmental Health Sciences in comparing the DES exposed with the 'control' group of non-exposed to learn what differences there may be in their health and reproductive histories.

All the subjects in this research are from the Dieckmann group: offspring of women at the University of Chicago outpatient maternity clinic given or not given DES in 1952. In this landmark study led by Dr. William Dieckmann and published in November 1953, the researchers concluded that "stilbestrol did not reduce the incidence of abortion, prematurity or postmaturity." Nevertheless, obstetricians continued to prescribe DES until the end of 1971.

The Dieckmann cohort is an excellent study group since they are all the same age and the mothers of the DES-exposed all received the same high dosage of DES. The first report from this study, covering the question of premature menopause, will be published in 1992.

### letters to the editor

Dear Editor,

I read the letter from D.K. in the Spring 1991 issue with great interest. She was interested in learning of other DES daughters with the vertebral problem called spondylolisthesis, which according to my medical dictionary is a forward subluxation (partial or incomplete dislocation) of the lumbar vertebrae on the sacrum. I am a 36-year-old DES daughter. After suffering a bout of lower back pain, I have recently been diagnosed with a different congenital, or birth, defect of my lumbar vertebra. I have congenital fusion of three lumbar vertebrae (L3-L5) and also have a sixth lumbar vertebra (typically there are only five lumbar vertebrae). Apparently, the three vertebrae never separated when my spine was developing. My orthopedic doctor tells me that he has never seen someone with three congenitally fused lumbar vertebrae in the 20 years he has been practicing. Fortunately, this defect has only mildly hampered my daily activities so far.

Like D.K., I would also be very interested in learning whether other DES daughters have congenital vertebral defects. Researchers have reported that estrogen receptors exist in bone cells (Komm et al, Science 1988; 241:81-4; Erikssen et al Science 1988; 241: 84-6), so that estradiol is now believed to have direct effects on bone. Whether synthetic estrogens like DES also have direct effects on bone is unknown. Congenital vertebral defects may prove to be another problem associated with DES



Dear Editor,

I was diagnosed as a DES daughter twelve years ago. At that time, I was told that I would not be able to have children. I was therefore very surprised when the pregnancy test I took last summer came back positive.

I had a textbook pregnancy—no complications. I now have a very healthy three-month old baby boy. My husband and I would like to share our story with my fellow DES daughters/sons. Enclosed is a picture of our cutie—Nathan Wade Goen.

Pamela P. Goen, Mt. Laurel, NJ

exposure, although it will be harder to study since detection of the problem requires that DES daughters receive X-rays that expose their lower back and pelvic areas to radiation. Collecting anecdotal evidence of congenital vertebral defects in DES daughters may be very valuable in deciding whether a more systematic study is warranted.

A.L.

Dear Editor,

In the Spring 1991 isssue of Voice there was a letter to the editor about birth defects, especially the spine. I too have spondylolisthesis Grade II. I have

often wondered about DES exposure and other birth defects. I also was born with my eyes crossed, underwent surgery at a year old, and now have no depth perception. Has any research been done on this? You may want to consider doing some sort of questionnaire about birth defects, other than ob/gyn problems. I have recently been diagnosed with a thyroid problem. Have there been any studies on DES and thyroid problems?

C.W.

Editor's note: DES Action is preparing a health history questionnaire that will appear soon in the Voice.

### **Anti-Secrecy Agreement Movement Grows**

onsumer rights activists and survivors of dangerous drugs and products are gaining momentum in efforts to bar "secrecy agreements" in out-of-court settlements. Settling lawsuits too often hinges on plaintiffs agreeing to never publicly discuss the details or reveal the terms of their court cases. Some DES daughters have signed such agreements because it is the only way they can obtain any compensation for their injuries. Secrecy agreements, however, benefit the pharmaceutical manufacturers by allowing them to avoid public scrutiny and the appearance of wrongdoing. Other DES daughters who

may be considering lawsuits are not able to learn about settlements and have a harder time assessing their chances for success.

The injuries caused by DES were discovered and made public by medical researchers and injured people themselves. For other drugs and medical devices, however, life-saving information has been withheld because of secrecy agreements. Corporations are able to continue selling products which have injured or even killed people because the record of destruction is sealed and protected by court order.

Last year the state of Florida

enacted the "Sunshine in Litigation Act" which forbids courts from entering orders which conceal a "public hazard" or information about a public hazard. The Texas Supreme Court established anti-secrecy guidelines in 1990 as well. Recently DES Action spoke in favor of an anti-secrecy bill which is moving through the California legislature, and similar legislative efforts are underway in many states. More and more people have become aware of the need to put the public interest above corporate interests. DES Action will continues to support legislation which advances the public's right to know.

The DES Research Symposium

# Looking Back, Looking Ahead

41-page transcript of the October 1989 presentations by:

Candice Tedeschi, R.N.C. "DES: The Basics"

Arthur Haney, M.D.

"Fertility Issues Associated with Prenatal Exposure to Diethylstilbestrol in Women."

Kenneth Noller, M.D.

"The DESAD Project and Recent Findings."

Sidney Wolfe, M.D.

"Where Do We Go From Here?"

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RESEARCH from page 1... funding was reinstated for one more year.

The Dieckmann study, a double-blind study on the effects of DES, has a cohort that was established 38 years ago at the University of Chicago. It remains a valuable opportunity to examine DES mothers and their children. Yet its funding is insecure and inconsistent.

The Herbst Registry, established by Arthur Herbst M.D. to investigate the pathogenesis and incidence of clear-cell cancer, is the largest record of clear cell cancer cases in the world. Yet it has not been funded since 1984.

Certainly the DES populations, who represent, among other things, an unprecedented model of transplacental carcinogenesis and drug-induced segulae, merit the sustained interest of the medical community. If we have learned anything from DES, it is to assume a latency period. Harmful effects are not always evident immediately. We cannot conclude that DES exposure has negligible risks because of evidence shown in a five or even fifteen year period of study. We must prove negligible risks after a lifetime of study.

Laboratory study after laboratory study shows that the effect of DES continues throughout the lifespan of the DES-exposed offspring. Animal and clinical studies show that the DES exposed have evidence of impaired immune systems and a higher incidence of autoimmune disease. Howard Bern Ph.D., whose animal studies on DES exposure show increased development of breast cancer at the mouse equivalent of middle age, said at a recent conference that "The age



"Many doctors do not know how little research exists on the DES-

exposed population.
They assume that if there is anything new to report they would hear about it.
But as there is so little research, how can there be information? And if there is scant information, how do doctors know what to look for in their patients?"

for the greatest potential hazard to the DES-exposed has not yet arrived."

Clear-cell cancer is still being diagnosed in 1991. The DES Cancer Network has learned of five new cases so far this year. It appears that the average age of diagnosis is rising. Arthur Herbst M.D. reports a clear-cell case diagnosed this year in a 41year-old woman. And he states the upper age limit for developing the cancer is unknown. Most worrisome is that anecdotal evidence has revealed late recurrences on the cancer happening from 8 to 20 years after initial diagnosis. As most cancers recur between one to five years after initial diagnosis, this is extremely unusual. Such a phenomenon has never been described in any other gynecological cancer. But because there are no studies. clinicians are unaware of the possibility of late recurrences. Data must be obtained and correlated with risk factors in a

prospective fashion.

In our DES Cancer Network, too many members have died from recurrence of the clear-cell cancer in the last year. I am frightened that we are the only ones aware of the incidence of recurrence. So, today, I am telling the world. Now you know too. In 1991, twenty years after the discovery of the link between DES and cancer, young women continue to die from DES related clear-cell cancer.

### **Government Responsibility**

There has always been a riddle about DES exposure. Who is responsible for the disaster? Who *will be* responsible to the population?

Over the years the NIH has funded various projects that look at one or another system affected by DES. Yet the problem of longitudinal studies on all groups has not been solved. Every NIH area, for the purpose of funding, is compartmentalized into organ systems or types of disease. Where is there a home for research on the DES-exposed population? What research model does DES fit? And is part of the problem of continued funding because DES does not fit an established system?

The new Office of Research on Women's Health can address the gaps in DES research by serving as the overseeing body, or nucleus, for DES research—varied components of which may come under its purview. The need, and the opportunity, remains for systematic government funding of epidemiological and biomedical research on the DES-exposed. This need can be met by this office, through an effort to find a creative solution to the uncom-

mon model of DES research.

### Underlying Attitudes and Myths

At one time there was a myth about the efficacy of DES during pregnancy. Are there other myths and underlying assumptions about the worth of DES research? It is important to examine this possibility because, as in so many areas of women's health research, attitudes influence action.

A familiar point in the life of a woman with DES related injuries is the time when she learns the history of DES. And she wonders how it can be that the story of DES is so little known. She wonders how it is that in 1991 thalidomide is still the most typical reference for an example of druginduced birth defects. And she cries out in a moment of recognition, "If this had happened to men the whole world would know about it!" What she means is that the terrible meaning of DES exposure would be understood. Action would be taken.

DES is often seen as a women's issue, creating the impression that DES affects only women and that it is *only* a women's issue. Is it possible that the minimization of concern about DES injuries reflects a cultural habit of dismissing women's concerns and devaluing women's experience of their bodies?

The DES-exposed are often told by their doctors that there is nothing to worry about—that the population is being watched. This myth holds that medical science is *naturally* looking after our population out of responsibility and scientific inquiry. Many doctors do not know how little research exists on the DES-

exposed population. They assume that if there is anything new to report they would hear about it. But as there is so little research, how can there be information? And if there is scant information, how do doctors know what to look for in their patients?

Another myth is that the DES story is over. It's been settled, it's been solved. On the contrary, the only thing that has been solved is the cause of injury. The full range of DES effects are still unknown. There are still mysteries to solve. In truth, DES is a classic example of a research topic that has lost status, while there is still scientific reason to investigate.

#### Benefits of research

In this era of chemical and environmental risk, DES research can not only provide answers about the DES-exposed, but can serve as a preventive model of:

- 🖁 a transplacental carcinogen
- adult and in-utero exposure to synthetic estrogens
- potential effects of Clomid and other fertility drugs
- late developmental and latent-occurring birth defects
- iatrogenic disease

In the broadest sense the DESexposed are information for posterity. Please don't let the injuries and concerns of 10 million people go to waste. Put what information our bodies can give to use by studying the whole picture of DES exposure.

Today, as I face you, my injuries, like the injuries of all DES-exposed, are invisible—but a constant in my life. I represent three generations of Americans who are hurt, scared, and scarred by a toxic prescription drug. I

represent the DES daughters who suffer repeated miscarriages, often at five and six months into their pregnancies. I represent the DES mothers who despair over their innocent decision, 20- to 50years ago, to take a drug prescribed by their doctor. Who wonder if they will have grandchildren. I represent the young women, diagnosed with clear-cell cancer in their early 20s, whose entry to womanhood is marked by the removal of their vagina and reproductive organs. I represent the DES sons who don't know what to expect as they age. I represent the hundreds of thousands of DESexposed people all over the world who rely on the research in this country to educate their governments and their physicians. And I implore you to investigate that which has not been addressed. To attend to a population that should never be forgotten.

I urge you to take a leadership role in prospective, not retrospective, studies. I urge you to:

1) promote a DES agenda for the NIH that will establish a research component on DES exposure,

2) insist on adequate funding for comprehensive research on the DES-exposed, and

 create a gynecologic oncology program whose mission it is to examine the DES population.

In this 20th year since the discovery of the link between DES exposure and cancer, I urge you to make a commitment to DES research. Please set an agenda that will keep us informed and will keep our eye on the ball. And the ball, ladies and gentlemen, is the future.



### books

Take This Book to the Gynecologist with You: A Consumers' Guide to Women's Health, a People's Medical Society Book by Gale Maleskey and Charles B. Inlander, Addison Wesley Publishers, 1991, \$9.95.

he chapters in this informative book cover: Before You Go; The Gynecological Settings: Inpatient/Outpatient Services; A Typical Visit; Procedures and Conditions; The Empowered Woman: Staying in Charge of Your Care; Keeping a Record.

### **Tribute Gift Program**

ou can honor a friend or relative for an anniversary, a birthday, as a memorial donation, or for any important occasion, by giving to DES Action in your honoree's name. If you would like to receive our Tribute Gift cards, please send us a note or call to let us know how many you would like.

### Correction

In the last **Voice**, we referred our readers to the American Medical Association for assistance in tracking down medical records of DES mothers. We need to qualify that referral. The AMA keeps records on all doctors in the U.S. for credential reference.

They will know a doctor's current address and the status of the practice. They do not have information on the location of a doctor's records. To locate a doctor, you can contact the AMA's Data Release office at 1-312-464-5199.

## **DES Action USA**

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