

Medical Reports

Reviewed by Pat Cody

Report on Third Generation Male Mice

"Proliferative lesions and reproductive tract tumors in male descendants of mice exposed developmentally to diethylstilbestrol" by Retha Newbold et al, *Carcinogenesis*, Vol. 21 No. 7, July 2000.

HERE is the companion piece to the study by Ms Newbold and colleagues that was published in 1998 and summarized in our Fall 1998 issue 78. That study concerned DES granddaughter mice, that is, the offspring of DES daughter mice. This new article is about the sons of DES daughter

mice, that is, grandson mice, the "third generation" when we count the DES mother as the first generation.

The results are equally dismaying. They found no reduction in fertility, but, as the male mice aged, they developed conditions not seen in a control group whose mothers and grandmothers were not exposed. A small number of these DES third generation male mice developed tumors in the rete testis and reproductive tract tissues. The authors write that:

"...the data in this report add increasing support to the idea that exposure to some chemical carcinogens may result in increased incidences of tumors in more than one generation of 'untreated' descendants."

From conversation with Ms Newbold, we learn that further studies are planned on the 4th generation—that is, the offspring of the 3rd generation daughter and son mice. Such work will definitively reveal whether DES exposure in utero can go down through the generations. ■

Non-clear-cell Cervical Cancer in Daughters

Janneke Verloop et al, "Prevalence of Gynecologic Cancer in Women Exposed to Diethylstilbestrol in Utero," *New England Journal of Medicine*, June 15, 2000. Vol. 342, No. 24, Correspondence Section.

RESEARCHERS at the Netherlands Cancer Institute analyzed questionnaires answered by DES daughters registered with the DES Information Center. The Institute received 5,421 replies from daughters whose median age was 30 years (range was 19-45 years old; DES was given later in Europe). In this group, a total of 111 cancers were reported by 105 women (clear-cell cancer

cases were excluded). This is triple the risk that would be found in non-exposed women of this age group. The authors write:

"DES daughters might actually be expected to have a lower prevalence of invasive cervical cancer than women in the general population, since DES daughters are screened more intensively for cervical cancer and since precursors lesions detected on screening are usually treated aggressively. Our finding is therefore particularly striking.

'Robboy and colleagues reported that the risk of squa-

mous-cell dysplasia and carcinoma in situ was doubled in DES daughters. They hypothesized that DES daughters might have an elevated risk of cervical cancer because of the presence of a wider transformation zone of metaplastic squamous epithelium, which might make them more susceptible to external carcinogenic factors. Larger studies...are needed to confirm our observations."

This report makes clear the need for DES daughters to continue their special DES exams for at least once a year for the rest of their lives. ■

Update on DES Internet Listservs

by Sally Keely (aka "DESxposd")

THERE are now several DES e-mail lists that you may be interested in joining!

DAL, the DES Action Listserv, is exclusively for DES Action members. This list is primarily informational and provides a direct link between DES Action staff and our members. To subscribe, send e-mail to DAL-request@telelists.com with the command "subscribe YourFirstName YourLastName" (without the quotes) as the only thing in the body of the message. Be sure you replace "YourFirstName" and "YourLastName" with the name under which your DES Action membership is listed. You will

receive a confirmation request to which you simply hit reply and send. If you have any problem, e-mail DAL-owner@telelists.com.

DES daughters should check out DES-L, the DES daughters listsev and online support forum at http://www.surrogacy.com/online_support/des/ To join the listserv, complete the online application and get ready to share support and information with 1000 other DES daughters!

DES sons will want to join the DES-Sons list for confidential discussions of issues related to DES exposure in males. This list was developed in conjunction with the DES Sons Network of DES Action. To subscribe send

blank e-mail to des-sons-request@egroups.com. Direct questions to des-sons-owner@egroups.com.

The DES-Family list welcomes all DES-exposed, their family, and friends. To join, e-mail listserv@sact.com with only the command "subscribe des-family" (without the quotes) in the body of the message.

Charli@egroups.com can help if you have questions.

Lastly, announcing the newest DES related listserv, DES-Pregnancies. DES daughters who are pregnant, trying to conceive, or contemplating pregnancy are invited to join via the list website <http://www.onelist.com/subscribe/despregnancies>. You will need to register with onelist, if you aren't already. Contact ladonnakat@aol.com if you have trouble subscribing.

Now, happy chatting!

DES Action Affiliates and State Contacts

DES Action Affiliates

Each affiliate was created and nurtured by volunteers. Write to them if you want information or would like to volunteer.

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610-16th Street #301
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desact@well.com

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DES Third Generation Network
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Seattle, WA 98112

State Contacts

State contacts participate in national projects organized by DES Action. Contact the national office if you would like to find out about our national projects.

Arizona
Los Angeles, CA
San Diego, CA
Grand Rapids, MI
New Jersey
New Mexico
Ohio
Oregon
Texas

DES Action International

Australia
Belgium
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England
France
Ireland
The Netherlands
New Zealand

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Notes from Nora

WE are thrilled to announce news that marks a true milestone. The Centers for Disease Control and Prevention have received full funding from the National Cancer Institute to carry out the National DES Education Program. At long last, the program we have worked towards for nearly ten years (and, truly, since DES Action's beginning in 1978) will begin. As with many important events, this announcement concludes one journey only to begin another.

During the next three years, a team of health care providers, consumer advocates, and public relations and public health professionals will work to design and carry out a national program to educate health care providers and the public about DES. We have been meeting in a Working Group since August 1999 to determine the fundamentals of this campaign. Now, with funding assured, we can move on to fine tune and then implement our program.

In this issue's "centerfold" we feature a poster developed by Stacey Hoffman, MPH, of the Centers for Disease Control and Prevention's National Center for Environmental Health. The poster depicts the stages of development thus far in our DES National Education Campaign.

We have been consistently impressed with the professionalism, dedication, and openness of the CDC staff and their sincere efforts to fully collaborate with the exposed population. Their approach has

revived our hope that a government agency could carry out a useful DES Education Program. As we now begin the real work of the education campaign, we want to thank all of our members for your role in bringing us to this point. Your letters to Washington, your financial support, and your words of encouragement have been invaluable. This is truly a victory for all those who care about the DES-exposed community.

Now the real work begins. The next step will be for the public relations and marketing experts at the firm of Porter Novelli to conduct focus groups among DES-exposed, non-exposed members of the public, and health care providers to test and sharpen the most effective messages we can use to inform our target audiences. Some of you may be hearing from us and invited to participate in a focus group or some other activity. If you do not hear from us, please do not feel left out. In general, the CDC will be concentrating initial efforts on those areas of the country that have been least served by previous public health campaigns. Anyone who is contacted will be mailed information directly from DES Action. No names will be provided to any outside organizations.

Again, thanks to all of our members who have made this exciting achievement possible. I look forward to reporting progress as the National DES Education Campaign develops. ■

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Developing a National Campaign to Educate the General Public

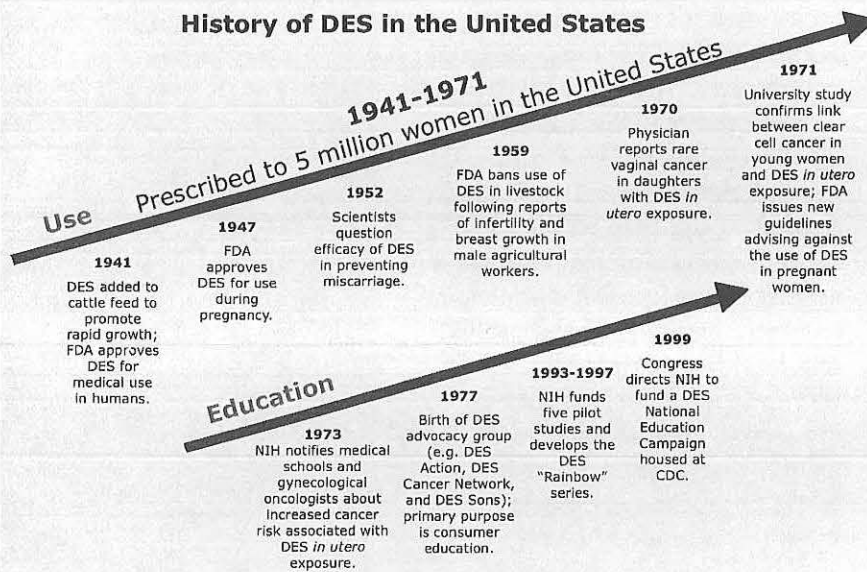
Stacey Hoffman
Centers for Disease Control
National Center for Environmental Health Effects Research

The author appreciates the support of the CDC DES Core Group: Judith Bass, Penelope Johnson, and others.

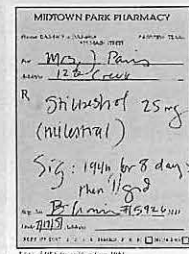


This poster was supported under a cooperative agreement from the Centers for Disease Control and Prevention.

History of DES in the United States

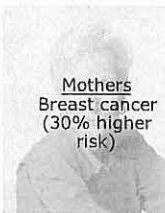


Potential Benefits of a National Consumer Campaign

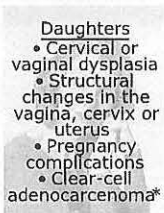


- Increase awareness among potentially exposed persons.
- Educate public regarding consequences of adverse adult health effects.
- Promote preventive behavior among exposed populations.

An Education Campaign for the General Public: Why Now? DES-Related Health Risks Continue into 21st Century



Mothers
Breast cancer (30% higher risk)



Daughters
• Cervical or vaginal dysplasia
• Structural changes in the vagina, cervix or uterus
• Pregnancy complications
• Clear-cell adenocarcinoma*



Sons
Testicular abnormalities

Animal studies in late 1990s have found increased risk for cancer in sons and grandchildren of DES-exposed mothers.

*Initially thought only to affect young daughters, recently discovered in daughters 40 years and older

Build a Strong Foundation (August-September, 1999)

Phase 1

- Hire professional staff.
- Invite internal partners from agencies with expertise in cancer, women's health, and managed care to join working group.
- Recruit working group of activists, scientists, and health care professionals with DES expertise and experience.
- Hold first working group meeting, and initiate discussion of campaign goals (August 30th).
- Initiate electronic list serve to facilitate communications with working group.

Education and Health Care Providers about DES (Diethylstilbestrol)

an, MPH
Control and Prevention
Environmental Health

son, Claudia Parvanta, Carol Rubin, Diana Swindel, Marsha Vanderford and Liza Veto.

se Control through the Association of Teachers of Preventive Medicine.

ATPM
Association of Teachers of Preventive Medicine

Potential Benefits of Provider Campaign



- Many providers are not fully informed or are misinformed about DES sequelae and appropriate preventive services.
- Providers must have up-to-date information to respond to questions from their patients about DES.
- Vigilant screening and early intervention can lower morbidity for DES Sequelae.

Ethical Considerations for a DES Education Campaign

- Heightened awareness may cause guilt for DES mothers.
- Heightened awareness may create anxiety for possible DES children (many of whom will be unable to confirm exposure).
- With heightened awareness, managed care agencies may move to consider the problem a pre-existing condition (and subsequently decrease screening/treatment benefits).
- DES education may compete with education for higher prevalent concerns for healthcare providers' time (e.g. heart disease, breast cancer).

The DES National Education Campaign

Identify Gaps and Establish Campaign Priorities
(October 1999-January 2000)

Phase 2

- Visit sites from five NCI pilot education studies.
- Meet with investigators, gather materials, and determine gaps and lessons learned.
- Hold second working group meeting. Review lessons learned from pilots, and finalize campaign priorities for service providers and the general public (January 27th).

Create a Campaign plan
(February-April 2000)

Phase 3

- Hire creative contractor.
- Work with contractor to develop audience segmentation analysis, proposal for formative research, and creative portion of campaign.
- Hold third working group meeting. Present campaign plan and gather feedback (April 26th).

What Happens Next?
(April 2000-?)

Phase 4

- Conduct formative research.
- Develop creative briefs for target audiences.
- Create strategic communications plan.
- Develop messages/materials and conduct concept testing.
- Complete product development/modifications.
- Develop materials dissemination plan.
- Develop plans to monitor campaign's ongoing progress, reach, and ethical impact.

Book Notes

Hormonal Chaos. Sheldon Krimsky, Johns Hopkins University Press, 2000, 243 pp.

By Judy Turiel

At first glance, the title of Sheldon Krimsky's new book, *Hormonal Chaos*, might lead you to expect yet another popular account of household life with an adolescent. But look at the smaller sub-title print—*The Scientific and Social Origins of the Environmental Endocrine Hypothesis*—and the more far-reaching scope of this book becomes apparent. The focus extends beyond anyone's day-to-day household to encompass lifelong, worldwide concerns. *Hormonal Chaos* presents a thorough analysis of the biological, health, political and economic dimensions of a current and profoundly important scientific hypothesis, one that raises crucial issues about government policy aimed at protecting the public.

Most of us might never pick up such a book, arising out of the academic community (Krimsky is a Professor of Urban and Environmental Policy at Tufts University). However, this "case study" of the relationship between science and public policy happens to be near to the heart, and to the lifetime experience, of DES-exposed women and men. Krimsky is looking at emerging evidence that chemicals related to DES, pervasive in our lakes, streams, and manufactured goods, are responsible for an array of long-term endocrine, developmental, reproductive and immune system problems ob-

"Hormonal Chaos presents a thorough analysis of the biological, health, political and economic dimensions of a current and profoundly important scientific hypothesis, one that raises crucial issues about government policy aimed at protecting the public."

served in wildlife and in humans. The DES connection explains my initial interest in *Hormonal Chaos*. Beyond that, Krimsky weaves a fascinating tale full of familiar characters (researchers like John McLachlan, Howard Bern, Retha Newbold, to name a few) and events. Particularly to my liking, he pieces together the big picture, a global puzzle in which DES-exposed people like me, and consumer organizations like DES Action, are a part.

Krimsky states the environmental endocrine hypothesis succinctly: "a diverse group of industrial and agricultural chemicals in contact with humans and wildlife have the capacity to mimic or obstruct hormone function—not simply disrupting the endocrine system like matter in a watchworks, but fooling it into accepting new instructions that distort the normal development of the organism." Krimsky traces three scientific paths from different research areas that have converged in this hypothesis:

- Discovery of long-term health effects from prenatal DES exposure in humans
- Studies linking wildlife reproductive disorders to industrial and municipal chemical waste and to agricultural pesticides
- Data suggesting a worldwide decline in the quality and quantity of human sperm (that one certainly caught the attention of media and the public!)

Krimsky begins his telling with biochemist Sir Edward Dodds' synthesis in 1938 of stilbestrol, that initial estrogenic compound that would soon appear as the drug DES prescribed to humans under various names and formulations, and as a food additive used to fatten livestock. The story moves on to Rachel Carson's *Silent Spring*, published in 1962, a book that raised the alarm about pesticides in the environment, particularly as cancer-causing chemicals whose potential damage extended to future human generations.

The spotlight of *Hormonal Chaos*, however, focuses on Theo Colborn, a wildlife biologist-environmentalist who played the pivotal role in developing and furthering research on the environmental endocrine hypothesis. Krimsky credits Colborn with integrating a daunting array of evidence from studies involving numerous animal species into a comprehensive scientific theory. The most significant and novel features of Colborn's framework

continued on page 8...

How Safe are Our Medicines?

Monitoring the risks of drugs after they are approved for marketing.

From DES Action Canada in collaboration with the Working Group on Women and Health Protection

MEDICINES have made enormous contributions to health....

However, all medicines also have side effects. These are effects other than the reason a drug is taken. They range from nuisance effects to serious, irreparable harm and even death. Some side effects may be common, others rare. Some medicines are riskier than others, but none are totally risk-free. That is why medicines should only be used if the expected benefits outweigh possible harm.

Last year, researchers at the University of Toronto published a study looking at how often people experience serious harmful drug reactions in hospitals, and how many people die each year as a result. They looked at U.S. hospital studies over the last 30 years, and only looked at deaths from normal medicine use, not overdoses or mistakes.

Their results were shocking. They estimated that between 75,000 and 100,000 people die from medicine use each year in the U.S. This would make harmful drug reactions the fourth to sixth leading cause of death. If their high estimate is correct, only heart disease, cancer and stroke claim more lives. At the same rate in Canada, between 7,500 and 10,000 people would die each year from taking medicines. All drugs have side effects. Deciding to take a drug is a balancing act, weighing possible benefits against possible risks.

Not enough known about new drugs

Our knowledge about the effects of new drugs is very limited. Usually, only 2,000 to 3,000 people have taken the drug in pre-marketing studies, often only for short periods of time. After it is released on the market, thousands or even millions of people may use the same drug. If 2,000 to 3,000 people take a drug, serious harmful reactions that occur in less than about 1 in 800 people are unlikely to be discovered.

"A lot of other potential health problems resulting from an adverse drug reaction go unreported"

Companies try to get drugs to the market quickly in order to get returns on the investments made in drug development. However, it is important to know that many of the new drugs marketed are not as valuable as we think. The evaluation of the Patented Medicines Review Board (Canada) states that between 1991 and 1997, of a total of 577 new patented products, only 50 (8.7%) were a real pharmacological breakthrough, 240 (41.6%) offered moderate, little or no advantage compared to products already available, and 287 (49.7%) were only "line extensions" of existing products (new dosage forms or other minor modifications)....

Current post-marketing surveillance practices catch only the tip of the iceberg

After they are approved for marketing, drugs are mainly

monitored through a system of voluntary adverse drug reaction reports which is not working very well. These reports are usually made by doctors, but can also be made by pharmacists and nurses, or even by the person suffering the adverse reaction. Companies are required to pass on all reports of serious harmful reactions to the Health Protection branch at Health Canada. A serious reaction is defined as one that caused a person to be hospitalized or stay in the hospital longer, or caused cancer, birth defects, disability or death.

A lot of other potential health problems resulting from an adverse drug reaction go unreported. Because filing reports is voluntary and not necessarily simple and straightforward, many doctors forgo the procedure. A study among family doctors in France compared the number of reported adverse drug reactions during a period of intense monitoring with a normal period and found that when doctors monitor intensely, they report 4,500 more serious harmful drug reactions than under normal circumstances....

The Five-Year Rule

Because so little is known about possible harmful effects of new medicines, a U.S. non-profit organization, Public Citizen Health Research Group recommends to its members:

"You should always wait at least five years from the date of marketing to take any new drug unless it is one of those rare breakthroughs that offers you a documented advantage over older proven drugs."

BOOK NOTES from page 6...

explaining adverse effects of certain environmental chemicals:

- the potential hazard is not only cancer, the focus of existing government regulations, but more various health, cognitive and behavioral problems
- effects are more pronounced, and troubling, for offspring of women exposed while pregnant and/or breastfeeding
- the concern is not only with high doses, acute toxic poisoning, but with the impact of low dose, chronic exposure

DES daughters do bear the dubious honor of reflecting the

"best documented effect" of an endocrine disrupter on humans—clear-cell adenocarcinoma of the vagina or cervix. As readers, therefore, we DES exposed are a jump ahead of the general public in understanding key evidence and concerns, in knowing just what Krimsky is talking about.

From his perspective, initial government actions are in motion, taken, as they must be, in the face of considerable scientific uncertainty and disagreement. As his concluding chapter summarizes so well:

"By the mid-1990s the environmental endocrine hypothesis had begun to invoke new metaphors of chemical risk, both within the scientific community

and among the general public...A number of human diseases whose causes were not well understood were beginning to be re-examined in terms of the mechanisms associated with endocrine disrupters. Among them were diseases of the male and female reproductive system, immune system, and thyroid gland, as well as breast and testicular cancers. Scientists devised animal models to study how a one-time chemical exposure in utero at the appropriate stage of embryonic development can result in irreversible abnormalities that may not show up in humans for decades." ■

22 YEARS OF

DES

ACTION

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