THE DES ACTION
VOICE
A FOCUS ON DIETHYLSTILBESTROL
Winter 1988 #35

Estrogen Replacement—Two Views

DES Action is receiving more and more questions from DES-exposed women about estrogen replacement treatment (ERT). Physicians now commonly prescribe estrogens to women whose endogenous levels (the estrogen their body produces) are low, especially following menopause. DES mothers may well have this treatment recommended by their doctor. In addition, DES daughters who undergo surgery for removal of their ovaries, and those with endocrine problems that result in chronically low estrogen, must also decide about ERT; in the coming years, all DES daughters will need to consider the pros and cons of ERT following menopause.

ERT raises questions of risks and benefits for any woman. For DES mothers and daughters, there is an additional question: Does previous exposure to the synthetic estrogen DES represent an added risk that must be weighed when later making a decision about ERT? *No one knows the answer.* The possibility that a "second exposure" to exogenous estrogen (estrogen from outside the body) might contribute to the development of cancer is suggested by animal research and by the demonstrated association between estrogens and certain cancers in humans. In 1978, a Federal DES Task Force issued the following statement about the use of estrogens by DES daughters: "In view of the lack of information on long-term effects of estrogens in these women (DES daughters) the committee felt that oral contraceptives and other estrogens should be avoided. The use of estrogens requires careful consideration by the patient and her physician of alternatives." A government press release said it would be "prudent" for all DES mothers or daughters to "avoid any further use of DES or other estrogens because the carcinogenic effects may be cumulative." DES Action has supported this cautious stand, especially in situations where effective alternatives do exist.

"In the coming years, all DES daughters will need to consider the pros and cons of ERT following menopause."

In recent years, considerable attention has focused on the relationship between osteoporosis (loss of bone density leading to risk of fracture) and low estrogen levels, and to the use of ERT to prevent, or at least slow the development of osteoporosis. Since bone fractures associated with osteoporosis can pose a serious

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INSIDE

1987 Annual Meeting

DES Action members from the U.S. and abroad recently gathered in San Diego for our 5th annual conference, this year entitled "DES: The Bigger Picture." The annual meeting is a time when active members meet to hear updates on medical research and legal information; learn new skills in such areas as fundraising, outreach, and publicity; share information of what their groups, both in the U.S. and other countries, have been doing; provide support to one another; and help to plan for future

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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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ANNUAL MEET *from page 1. . .*
direction of the organization.

Attendees included representatives from local DES Action chapters across the U.S. (including our two newest locals in Oklahoma and Washington), both mothers and daughters from the DCN (DES Cancer Network), coordinators of our international affiliates from Canada, the Netherlands, and our newest group in France, state health department representatives, board, and staff.

Highlights of the meeting included:

- moving and inspiring personal stories from the largest yet assembled group of DCN mothers and daughters
- an exciting brainstorming session on our upcoming national media campaign
- plans by our international group to work with the European parliament to have DES removed from listings of approved medications
- a group discussion of DES as part of the bigger picture of medical and reproductive technology and practice and where we see our role as an organization in the upcoming years on these issues

Future VOICE issues will include additional information that was presented at the conference that may be of interest to you, our readers.

VOICE

DES Action Represented at Gordon Research Conference

by Judy Turiel, Research Liaison

In August DES Action was represented at the Gordon Research Conference on "Hormonal Carcinogenesis"; a 5-day conference, tucked away at a New Hampshire prep school, which brought together nearly 100 scientists from the United States and abroad for informal "off-the-record" discussion of current research. Participants were primarily basic scientists who are trying to understand the role of hormones (especially estrogens and androgens) in the development of cancer. Many of them have used DES, as well as other estrogens, in their experiments with laboratory animals and/or cell cultures. (Interestingly, some participants were drug company researchers working on new applications of hormones for various health conditions.)

Information on hormone-related cancer in humans was provided by Arthur Herbst, who discussed DES exposure, and Robert Hoover, from the National Cancer Institute, who presented an epidemiological perspective on human reproductive tract cancers. DES Action also represented the human dimension of hormonal carcinogenesis at the conference "poster session", where a participant provides information visually, on a poster, rather than through a lecture. DES Action's poster, entitled "DES Exposure in Humans: An Unfinished Experiment", summarized known health consequences of human DES exposure, questions that need further research, and the role DES Action plays in addressing this public health problem.

Gordon Research Conferences on a wide range of specific scientific topics are held throughout the summer at various schools in New Hampshire and Rhode Island. DES Action's invitation to participate in this highly regarded conference arose from contacts we have established with basic scientists involved in DES-related research. Such interactions with the scientific community are extremely valuable, as they enable us to better understand the painstaking process of accumulating knowledge about DES exposure, and to gain insights into current theories, controversies and uncertainties that exist. At the same time, we think it is valuable for scientists to be reminded of the health outcomes in men and women—the real-life human consequences that often seem remote from experimental laboratories.

CORRECTIONS

In the last issue of the VOICE, two errors appeared in the "Medical Reports on Fertility" article. They should read as follows:

Paragraph one, sentence one: In some cases, for example, when a tubal pregnancy has reached the emergency stage and must be removed immediately, there is not time to discuss whether to have tubal surgery and if so, what type.

Paragraph one, last sentence: Remember, there is no recommended surgery for DES-associated tubal abnormalities to prevent tubal pregnancy or to improve chances of conception.

Additional medical reports on ectopic pregnancy will be discussed in the next issue of the VOICE.

Save Money and Help DES Action!

Enclosed in your present issue of the VOICE you will find an application for a VISA card. This "One Card" is provided through the Grantsmanship Center, a national non-profit organization that lends technical assistance to other non-profits on fundraising. This VISA card's annual fee of $21 is lower than most, as is its annual percentage rate (13.75% or 16.75% depending on the plan you choose). In addition, for every new member who receives this VISA card (and in years after, for every renewed member) DES Action receives $7. Thus, you can save money and help DES Action in the process! If you are interested in additional brochures for family and friends, please contact the national office in San Francisco. Thanks in advance for your support!

ESTROGEN *from page 1. . .*

health risk, information about the value of ERT for this condition becomes a significant aspect of a woman's decision regarding estrogen use. Studies of ERT and its relationship to osteoporosis and other health conditions are accumulating, but do not point to definite conclusions. Given the controversy and disagreement that surround ERT, DES Action asked two physicians to summarize their interpretations of current information and their opinion about ERT for DES-exposed women.

Specific questions we asked were:

- What clinical testing is used to determine if a woman needs ERT?
- Is the newly approved estrogen skin (transdermal) patch a better way to administer estrogen to DES daughters who have had surgery for clear-cell adenocarcinoma, including removal of their ovaries?
- How long has the estrogen skin patch been tested?
- Have the risks vs. benefits of any type of ERT been assessed for DES mothers and DES daughters?

We selected physicians who might have differing perspectives on these questions. We present their views in the spirit of ongoing inquiry, not definite answers. Research continues on the relationship between hormones and cancer (see p. 3, Gordon Conf.). Today's medical opinions may change as more studies lead to greater understanding of this relationship.

While ERT may be appropriate for certain individuals, one risk of this treatment is that it will be prescribed routinely to many more women than is justified by a careful weighing of risks and benefits in individual cases. *The following responses indicate that, unfortunately, current medical research on ERT does not include studies specific to DES-exposed women.* As further information becomes available, we will continue to address this important and perplexing issue of estrogen replacement treatment.

Response by Sadja Greenwood, M.D.

Assistant Clinical Professor
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Clinical Testing

Clinical testing to determine if a woman needs estrogen therapy is still in its infancy. Estrogen may be given to women who are suffering from hot flashes or for the relief of vaginal dryness and soreness with intercourse. In both these cases the hormone is generally given because a woman is uncomfortable. However, in the case of osteoporosis (brittle bones which fracture easily with aging) testing would be helpful to predict who is most at risk. About 25% of White and Asian women develop osteoporosis, usually after the age of 60, while Blacks and Latinas are less at risk. Screening tests for bone density are not yet precise enough to give valid answers about osteoporosis or the likelihood of fractures. Laboratory tests of calcium excretion in the urine and other markers of bone breakdown have not been thoroughly worked out.

When considering ERT, doctors and postmenopausal women are still best advised to see whether an individual has known risk factors for osteoporosis — such as low body weight, small muscle mass, smoking, high alcohol use, sedentary life style, and low calcium intake over the years. Long-term use of cortisone, dilantin or high doses of thyroid may also predispose towards osteoporosis. Osteoporosis and fractures are decreased markedly in severity if estrogen is taken after the menopause.

Skin Patch vs. Pills

The administration of estrogen via a skin patch has been studied in Europe and the United States by the Ciba-Geigy Corp. since the early 1980s. Taking estrogen in this form, in which the hormone is gradually absorbed at a steady rate, allows for a more even blood level of hormone than is found when a woman takes a pill once every 24 hours. The significance of this is not known, but it is probably more physiologic—that is, similar to the situation when the ovaries secreted estrogen on their own. The patch also allows the woman to take a lower dose of estrogen than she would if she took the same compound in pill form, since hormone is not "lost" by passing first through the intestinal tract.

When an estrogen pill is taken by mouth, it is absorbed by the intestinal blood vessels and carried to the liver, where it is metabolized or "processed." One of its effects on the liver is to

elevate a protein that can cause a rise in blood pressure in susceptible women. Because the estrogen patch does not have this effect, the patch may be the best estrogen choice for women with a personal or family history of high blood pressure. On the other hand, estrogen pills also cause the liver to change cholesterol levels in a favorable direction, raising the HDL cholesterol fraction that seems to be protective against heart disease while lowering total cholesterol. Since the estrogen patch does not seem to have this favorable effect on cholesterol, its usefulness may be lessened.

At present, most doctors feel that the estrogen patch is a new way to administer estrogen that may have advantages for some women, such as those with hypertension; other purported advantages and disadvantages remain to be worked out. Some women subjectively feel better with the patch and others with estrogen pills. Some do not like either form of estrogen. The patch is more expensive than oral tablets, and some women develop a skin rash at its area of application.

As far as DES daughters are concerned, there is no current evidence that the estrogen patch is a better way to administer estrogen replacement, if such replacement is desired.

Risks vs. Benefits

Many women have lived to a healthy old age without taking estrogens after menopause. Others are helped by these hormones. Estrogen has some benefits, as outlined above, and some known risks, including a greater risk of uterine cancer unless it is taken with 10 to 14 days of progesterone each month, and an increased risk of gall stones requiring surgery.

For DES mothers, the question of breast cancer risk arises. One recent study showed DES mothers have approximately a 40% increase in risk of developing breast cancer 20 years after taking DES. There are many risk factors involved with the development of breast cancer, including family history, pregnancy history, diet, weight and alcohol use. Estrogen use after the menopause may or may not be another risk factor for breast cancer; most studies do not seem to show this but some do. In many animal studies of breast cancer sex hormones do "promote" the growth of tumors.

"For DES daughters, there is no current evidence that the estrogen patch is a better way to administer estrogen replacement."

DES mothers should do breast self exams, see a good clinician regularly and have low-dose mammograms every two years after 40 and yearly after 50. If they decide to take postmenopausal estrogens they should follow these same precautions.The choice for a DES daughter with regard to postmenopausal estrogen is not different from the choice for any other woman, as far as we know. It is an individual choice,which should be made by a woman and her clinician after both find out as much as possible about her needs and risks.

Response by
Steven J. Ory, M.D.

Associate Professor
and Chairman
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Past Problems With ERT

Few issues in gynecology have created as much controversy and confusion as estrogen replacement therapy. Exogenous estrogen has been prescribed for over 100 years for a variety of reasons. Its indiscriminate use in the past has led to two enormous problems—the development of two very different cancers. One type of cancer is associated with estrogen use during pregnancy: clear cell adenocarcinoma of the vagina in young women exposed to DES in utero. Additional exposure to DES or any other estrogen after the time of organ development in fetal life is not known to be associated with any type of vaginal cancer.

The second cancer associated with estrogen use is endometrial cancer (cancer of the uterus). This type of cancer is seen in women prescribed estrogen because their own estrogen levels are low. The association of estrogen and endometrial cancer was conclusively documented about 11 years ago; any type of estrogen is capable of producing cancer of the uterus if given for a long enough time, at a high enough dose. However, a number of studies demonstrate that the potential cancer-causing effects of estrogen can be blocked by another ovarian hormone—progesterone. If progesterone is given to women who are not ovulating

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ESTROGEN *from page 5. . .*
—the majority of women on ERT—the risk of endometrial cancer is less than in the population at large.

Estrogen Deficiency and Osteoporosis

Recently, there has been increased awareness of the consequences of estrogen deficiency, especially at the menopause. Following a decline in estrogen levels, women experience three types of symptoms that are directly related to inadequate estrogen: hot flashes and associated vasomotor symptoms (this involves constriction or dilation of blood vessels), thinning and discomfort of the vaginal tissues, and osteoporosis. Osteoporosis is a decrease in the amount of calcium in the bones, and is the menopause symptom that concerns us the most. If the amount of calcium in bones (bone density) falls below a critical level, an individual becomes susceptible to bone fractures. In particular, compression fractures of the spinal column, hip fractures, and fractures of the forearm are common in menopausal women. Bone loss can be prevented by taking estrogen, but this treatment is effective only as long as it is given. Bone loss resumes as soon as ERT is stopped.

"Our current feeling is that there are no contraindications to (reasons against) ERT in DES-exposed women, but the risk versus potential benefit should be evaluated on an individual basis."

Osteoporosis is a problem of enormous proportions in this country. It was recently estimated that 1,200,000 osteoporosis-related fractures occur in the elderly each year, including over 500,000 spinal fractures and 27,000 hip fractures. The total health care cost related to osteoporosis exceeds $7 billion annually in the United States alone. Illness and death associated with osteoporosis exceeds that of all gynecologic cancers combined.

Preliminary evidence suggests that ERT may also slow the development of cardiovascular (heart and blood vessel) disease in women. If true, the potential benefit would be even greater than the prevention of osteoporosis.

Thus we are recommending ERT to an increasing number of women. ERT is safe and beneficial if given with a synthetic progesterone drug (a "progestin") and calcium. We have recently learned that calcium alone is not adequate to prevent osteoporosis, but it is an important addition to ERT.

There are many different types of estrogens which have in common their ability to produce "estrogen effects." Some are "natural" estrogens which are identical to estrogens normally produced by the ovary (estradiol is the major estrogen made in the ovary). Others, including DES, are chemically very distinct from natural estrogens, and may produce effects beyond those of the natural estrogens such as effects seen in DES offspring. We do not know precisely how these synthetic estrogens may produce these different effects.

The Skin Patch

One product that has been tested for seven years and recently introduced in clinical practice is the estradiol skin patch. A possible benefit of this method is that it allows a continuous source of estrogen, much as it is normally produced by the ovary. Additionally, a lower level of

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Additional Information on Menopause and ERT

If you would like additional information on our cover article topic, the following is a list of suggested readings:

- *Growing Older, Getting Better*, Jane Porcino, Addison-Wesley, 1983, $12.95.
- *Menopause, Naturally: Preparing for the Second Half of Life*, Sadja Greenwood, M.D., Volcano Press, 1984.
- *Midlife Health—Every Woman's Guide to Feeling Good*, Ada P. Kahn and Linda Hughley Holt, M.D., Facts on File Publications, 1987.
- *Our Selves, Growing Older*, Paula Brown Doress and Diana Laskin Siegal of the Midlife and Older Women's Project in cooperation with the Boston Women's Health Book Colletive, Simon and Schuster, 1987, $15.95

Meet Our New Board Members

The following three women were appointed to the DES Action USA board of directors at the fall meeting in San Diego. We welcome them and the unique skills that each brings to the group.

Candice Tedeschi

Candice Tedeschi is a nurse practitioner specializing in women's health care. She is coordinator of the DES Screening Center at Long Island Jewish Medical Center in New Hyde Park, NY. Candy joined the nursing staff at LIJ in 1975 as an RN in the neonatal intensive care unit. In 1979, she began work as a nurse clinician for Dr. Burton Krumholz, Associate Director of OB/GYN at LIJ.

Candy is frequently interviewed on the subject of DES and its effects by print and broadcast media. The mother of three girls, Candy and her husband live in Roslyn, NY.

Joyce Bichler

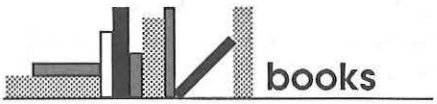
Joyce was recently reappointed to the DES Action board after a one-year hiatus. She is a founder of DES Action Minnesota, DES Action Hudson Valley, and the DES Cancer Network.

Joyce's involvement with the DES issue started abruptly when in 1972 she learned that she had clear cell adenocarcinoma. Joyce was unexpectedly thrown into the public spotlight when she became the first DES daughter in the country to successfully sue the pharmaceutical industry for marketing DES. Joyce's book, *DES Daughter: the Joyce Bichler Story* soon followed, detailing her experiences as a DES cancer daughter and litigant.

When not involved in DES matters Joyce is employed as a social worker and counsels physically disabled adults at a rehab center in Kingston, NY.

Libby Saks

Libby was appointed to the DES Action board of directors again after a two-year leave. She initially joined the national board in 1979 and has remained an integral part of the organization since that time. She has overseen the operations of our east coast office at the Long Island Jewish Medical Center for the last ten years, working with our two staff people in that office to coordinate membership information and provide educational materials and referrals to the membership and the general public about DES.



Fertility Awareness

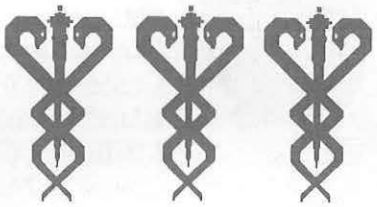
Three booklets are available on this topic, which the publisher describes as "not the rhythm method" but as a system of checking and charting daily changes in cervical mucus, basal body temperature and cervix condition and quality. The booklets are *The Ovulation Method Charting Booklet* ($6.50), *The Ovulation Method/Natural Family Planning Class Outline* ($12), and *Infertility Trouble-Shooting: Self-Help Suggestions for Regaining Fertility* ($8.95). Send orders to Small World Publishers, Box 305, Corvallis, OR, 97339.

ESTROGEN *from page 6. . .*
estrogen can be maintained in the blood when the hormone is absorbed through the skin. The estrogen patch is an attempt to provide a more physiologic (closer to the body's own) method of estrogen replacement. However, since ERT by pill with other natural estrogens is extremely safe when given with a progestin, it will be difficult to demonstrate any significant advantage of the patch over other forms of ERT.

Who May Need to Consider ERT?

Three groups of DES-exposed women may need to consider ERT: 1) Older women facing normal menopause, 2) Young women with premature menopause (surgical or not), and 3) Women with very low endogenous (their own body's) estrogen production even before menopause, due to some type of chronic endocrine imbalance (for example, related to continuous strenuous physical activity). It does not appear that the incidence of low endogenous estrogen production (hypothalamic, or "runner's" amenorrhea) or premature menopause is increased in DES daughters. ERT has been utilized in these women, and there are no reports of progression of any DES-related abnormalities. However, no systematic studies have been done on estrogen use by DES daughters.

Our current understanding of estrogens and our clinical experience with ERT in general offers considerable reassurance that there will be no problems related to ERT. However, this is an issue that will be intensively studied as the population of DES-exposed women approaches menopause. Our current feeling is that there are no contraindications to (reasons against) ERT in DES-exposed women, but the risk versus potential benefit should be evaluated on an individual basis. If ERT appears to be justified for an individual, it is my opinion that it should not be denied because of her DES exposure.



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