

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

TO : Public Health Service (BCHS) Grantees

DATE:

NOV 30 1978

FROM : Regional Health Administrator, PHS
HEW Region IX - San Francisco

SUBJECT: Bureau of Community Health Services (BCHS)
Diethylstilbestrol (DES) Task Force Report

The DES Task Force established at the request of Secretary Califano in February 1978, has just completed and submitted its report.

As a result of the findings, the Task Force concluded that full disclosure of information to health professionals and potentially at-risk individuals concerning DES use in a past pregnancy is essential to protect the health of at-risk women and their children. The Secretary is, therefore, taking two major steps to implement the recommendations:

1. A major program to alert physicians and other health professionals to the findings and recommendations of the DES Task Force; and
2. A public awareness program targeted at exposed individuals. The program will emphasize the importance of early detection in improving the possibility of successful treatment of cancer and other abnormalities that may result from DES exposure.

In broad outline, both physicians and exposed individuals will be told the following:

1. Daughters should begin periodic screening examinations at age 14 or at the onset of menses, whichever occurs earlier.
2. Mothers should advise their physicians that they were exposed and should follow a system of regular examinations.
3. Sons will be urged to see a physician for an examination to determine if they have genital abnormalities associated with DES exposure.

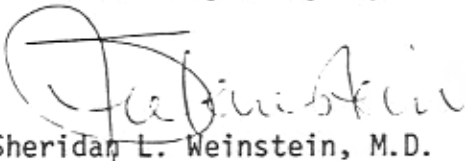
4. It is prudent for all DES-exposed women -- mothers or daughters -- to avoid, when possible, any further use of DES or other estrogens because the carcinogenic effects may be cumulative.

Therefore, all BCHS grantees are advised to:

1. Seek and record information related to patients' exposure to DES;
2. Follow the PHYSICIAN ADVISORY (Attachment A) in their management of patients; and
3. Maintain a patient subfile on DES users or children of DES users. The subfile can be a list of patient names/numbers for tracing patients, if necessary.

Since it is prudent for all DES exposed women -- mothers or daughters -- to avoid, when possible, any further use of DES or other estrogens because the carcinogenic effects may be cumulative, all family planning clients seeking oral contraceptives should be questioned carefully regarding prior DES exposure. If a client has been exposed, the Program should follow the recommendations contained in the PHYSICIAN ADVISORY.

The statement by the Secretary on the DES Task Force Report and health risks associated with use of DES is also provided for your information (Attachment B). Please share this information and the PHYSICIAN ADVISORY with appropriate staff and delegate agency providers.


Sheridan L. Weinstein, M.D.

Attachment



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
OFFICE OF THE ASSISTANT SECRETARY FOR HEALTH
WASHINGTON, D.C. 20201

October 4, 1978

PHYSICIAN ADVISORY

Health Effects of the Pregnancy Use of Diethylstilbestrol

Diethylstilbestrol (DES) is a synthetic estrogen first produced in 1938. It has since been used for a wide variety of medical conditions, including prevention of pregnancy complications from the 1940's until 1971 when the Food and Drug Administration (FDA) required product labeling to state that DES was contraindicated for use in the prevention of miscarriages.. It is estimated that 4 to 6 million Americans (mothers, daughters, and sons) were exposed to DES during pregnancy. Although DES is a synthetic estrogen and differs in structure and metabolism from naturally occurring estrogens, many investigators believe that there is no evidence that natural and synthetic estrogen differ in biologic effect (including toxic effects).

Studies have shown a clear association between the occurrence of a rare form of malignant vaginal cancer, clear cell adenocarcinoma, with intrauterine exposure to DES. In addition, many DES daughters were found to have a benign vaginal condition called adenosis. This condition is characterized by the presence of non-malignant glandular tissue in the vagina.

More recently, a follow-up study at the University of Chicago revealed more breast and gynecologic cancers among exposed mothers than among a control group, although the difference was not statistically significant. A follow-up of DES mothers at the Mayo Clinic did not reveal any increases but the dose of DES was on the average lower in the Mayo Clinic group.

In addition, recent studies have shown an excess of abnormalities in the genital and possibly lower urinary tract in DES-exposed males. A DES Task Force was formed in February by the Office of the Assistant Secretary for Health to examine the health effects of DES in pregnancy. The group examined the current state of medical knowledge concerning the drug's effects and made recommendations for immediate action as well as future research. This Advisory outlines the Task Force's recommendations to assist you in managing your patients who may have had pregnancy exposure to DES.

NOTIFICATION

The Task Force recommended that all involved persons be informed of their exposure. While recognizing difficulties (search of old medical records and locating patients who move from the area of obstetrical care), the Task Force recommended that physicians should:

- o Notify women to whom they prescribed the drug of their exposure and advise them about the need for follow-up medical care for themselves or their offspring.
- o Check their medical records carefully when approached by patients inquiring about possible past exposure to DES in order to provide these patients with information as accurate and complete as possible.
- o Provide this information without charge to the patient.

The Task Force wishes to emphasize that full disclosure to patients of information concerning DES use in a past pregnancy is essential to protect the health of the patient and her children.

DES DAUGHTERS

The incidence of clear cell adenocarcinoma is estimated to be between 1.4 per 1,000 and 1.4 per 10,000 in exposed daughters which is less than originally feared. Although some DES daughters have both adenositis and clear cell adenocarcinoma, the progression of adenositis to carcinoma is suspected in only 2 or 3 instances.

Active therapeutic intervention (i.e., surgery, such as vaginectomy, excision, or radiotherapy) for adenositis is not recommended but these patients should be followed by repeated examinations.

The recommended examination of asymptomatic DES daughters is as follows:

- o Periodic screening examinations should begin at age 14 or at menses unless there is vaginal bleeding or discharge. If present, such bleeding or discharge calls for prompt evaluation.
- o The screening procedure should be a thorough pelvic examination including Papanicolaou smear and iodine staining (one-half strength aqueous Lugol's solution). Non-stained areas of the vagina may indicate adenositis.
- o DES daughters should be examined once a year. More frequent examinations may be required for cases with extensive epithelial changes.

- o Colposcopy should be used selectively for examination of DES daughters. Colposcopy should be utilized (a) in all cases of abnormal cytology (Papanicolaou smear), (b) where feasible as part of the initial examination, and (c) in cases of extensive epithelial change such as squamous metaplasia. Biopsies should be reserved for more specific indications.

Sufficient information is not available to document fertility rate, pregnancy outcomes or long-term effects on offspring of DES mothers.

Hysterosalpingography is not recommended as a routine screening procedure in DES daughters. It should be reserved for cases in which repeated pregnancy loss or infertility occurs. There should be a thorough discussion of this procedure by an informed patient and her physician.

DES MOTHERS

Recent studies led the Task Force to express serious concern about the carcinogenic potential of DES in women who took the drug during pregnancy. The Task Force concludes that a relationship between DES exposure during pregnancy and the risk of breast or gynecologic cancer in the mothers is not established but is suspect. Accordingly, the Task Force recommends that studies be organized or expanded to clarify this issue.

Asymptomatic DES mothers should be urged to follow a system of routine screening which would be considered appropriate for women without prior estrogen exposure.

If the increased risk is confirmed, the cancer may appear at an earlier age than is usual for breast cancer (i.e. within 20 years after exposure to DES). Asymptomatic DES mothers are urged to follow these medical care guidelines:

- o Have an annual pelvic examination including a bimanual palpation and Papanicolaou smear.
- o Undergo a breast examination that follows current National Cancer Institute guidelines for breast cancer screening.

These call for:

- a. Monthly breast self-examination and the report of any abnormal findings to their physicians.
- b. Annual palpation of the breasts by qualified medical personnel.
- c. No mammography under age 35 for routine screening.
- d. Between 35-39 annual mammography only if the woman has a personal history of breast cancer.

- e. Between 40-49, annual mammography examination only if a woman has a history of breast cancer in immediate relatives (mothers and sisters) or a personal history of breast cancer.
- f. Over age 50, annual screening mammography examination may be considered.
- g. The Task Force is concerned about the use of X-ray mammography as a screening modality in DES mothers under 50 years of age. This concern relates to (1) lack of proven benefit of such screening in these younger women, (2) presumed risk of radiation, and (3) experimental work suggesting an interaction between DES and radiation.

With any signs or symptoms suggestive of breast cancer, a diagnostic workup, which may include mammography, is indicated:

DES SONS

Findings of clinical studies include an increased frequency among DES-exposed males of: (1) a history of cryptorchidism, (2) hypoplastic testes, (3) epididymal cysts, and (4) abnormalities such as low sperm counts, decreased motility and possibly abnormal sperm forms. As yet, there is no definitive information on the fertility implications of these findings. The Task Force concluded that additional studies are needed to evaluate the possibility of an increased incidence of testicular cancer among men exposed to DES in utero.

Recommendations for DES-exposed sons are:

- o Young boys and men exposed to DES in utero should be advised to undergo a physical examination to ascertain if they have abnormalities associated with DES exposure such as undescended or hypoplastic testes.
- o Undescended or hypoplastic testes require medical follow-up or corrective measures. Even in cases where there has been no DES exposure, undescended and hypoplastic testes are well recognized conditions which predispose to testicular malignancy.
- o Testicular self-examination is safe but unproved as a satisfactory screening technique. It has been recommended by some physicians and consumer groups.

PSYCHOSOCIAL IMPLICATIONS

Anecdotal reports indicate that some DES-exposed persons experience some degree of psychosocial problems. Although research is required to document such changes, physicians must be alert to the occurrence of such problems, especially in teenagers or young people and provide appropriate recommendations for counseling.

USE OF DES FOR POSTCOITAL CONTRACEPTION

Although the doses and duration of DES use for postcoital contraception are less than the doses and duration which were commonly used when DES was prescribed for pregnancy complications, health risks may be similar. It also is possible that women may take the drug as a postcoital contraceptive when already pregnant from previous intercourse. In such cases, the potential offspring of such pregnancy would be exposed to the risks previously described. Additionally, there is controversy over the efficacy of the drug for postcoital contraception and over the validity of studies showing it to be effective for that purpose. In light of these considerations, the following recommendations are made:

- o Postcoital contraception with estrogens in any woman should be restricted to situations where no alternative is judged acceptable by a fully informed patient and her physician.
- o Thorough birth control counseling should accompany or follow any prescription of estrogens for postcoital purposes. A principal objective of such counseling should be to discourage women to whom the drug is administered from considering it as a routine method of contraception upon which to rely in the future.

FURTHER ESTROGEN USE BY DES-EXPOSED WOMEN--OFFSPRING AND MOTHERS

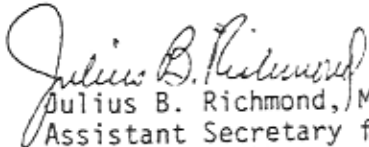
The Task Force believes the use of DES and other estrogens should be avoided when possible by DES women. The following are specific recommendations:

- o Physicians who are considering prescribing DES, or other estrogens, for postcoital purposes should inquire whether the individual has had prior pregnancy-related exposure to DES. If the drug is prescribed for an individual previously exposed in utero, she should be counseled concerning the heightened importance of avoiding any future use of the drug for postcoital purposes.
- o The use of oral contraceptives and post menopausal replacement estrogens, though not contraindicated, must be viewed in a prudent fashion, and the decision to use them made only after careful consideration of alternate methods, patient preference, and medical judgment.
- o DES should not be used to suppress lactation in DES-exposed women. The FDA is in the process of withdrawing DES for use to suppress lactation.

Most DES-exposed persons will suffer no serious, long-term effects. Hopefully, your patients will have no ill effects. The Task Force Report will be published soon in its entirety. In the Department of Health, Education and Welfare's plan for follow-up to the report, a number of articles will be published and seminars and training courses will be held.

For further information, or a copy of the Task Force report, you can write to the Office of Cancer Communciations, National Cancer Institute, NIH, 9000 Rockville Pike, Bethesda, Maryland 20014.

Sincerely yours,

A handwritten signature in cursive script, reading "Julius B. Richmond".

Julius B. Richmond, M.D.
Assistant Secretary for Health and
Surgeon General