CARING FOR THE DIETHYLSTILBESTROL EXPOSED PATIENT

DES Mothers, DES Daughters, DES Sons, DES Grandchildren, & DES Exposed

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DES INFO ASSOCIATION & DIETHYLSTILBESTROL (DES) INTERNATIONAL INFORMATION AND RESEARCH GROUP
DESInfo411@gmail.com *Karen Fernandes, R.N., CPHQ* **desexposed@gmail.com** *Scott Kerlin, Ph.D.*
Reference Page: grad-mentor.com/des-research
Facebook: DES (Diethylstilbestrol) Info & DES Research and Support Group of Dr. Scott Kerlin

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DES Info Association & Diethylstilbestrol (DES) International Information and Research Group
DESInfo411@gmail.com *Karen Fernandes, R.N., CPHQ* DESExposed@gmail.com *Scott Kerlin, Ph. D*
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Overview & History of DES (Diethylstilbestrol)
Care Needed for the DES Population

This is a guide to assist you in caring for your Diethylstilbestrol (DES) Exposed Patient. They either took DES, were exposed in-utero or are a 3rd/4th generation.

DES (Diethylstilbestrol) is a synthetic estrogen given as an anti-miscarriage drug to millions of pregnant women, primarily from 1938–1971, but not limited to those years. It was also given to mothers to dry up their milk after delivery, as a morning-after pill to prevent pregnancy or to stunt the growth in young girls.

The DES Exposed population are at risk for certain reproductive cancers, reproductive malformations, infertility/pregnancy problems along with depression. A number of health conditions have also been noted along with genetic changes.

Patients: Please share this information with your physicians and health care providers

This report contains a sampling of the large number of published research studies on DES which verify the importance of continued vigilance for health and medical risks.

DES Timeline *(Research References: grad-mentor.com/diethylstilbestrol-multigenerational)*

- **1938:** The story of DES began**,** when British physician and chemist Sir Charles Dodds and his team of scientists synthesized DES from a coal-tar derivative. DES, the first synthetic oral form of estrogen, mimicked the effect of natural estrogen
- **1940:** French medical journal reported that DES caused mammary tumors in male mice
- **1947:** FDA issued a marketing authorization for DES as a treatment to prevent miscarriages
- **1950:** Research revealed that DES was used to treat over 100 medical conditions
- **1953:** Dieckmann study at the University of Chicago concludes that DES "has no beneficial effect whatsoever on the prevention of miscarriage." (*American Journal of Obstetrics and Gynecology*)
- **1962:** FDA declares DES ineffective for protecting pregnancy
- **1970:** Clear Cell adenocarcinoma vaginal cancer found in teenage girls exposed to DES in utero. The risk continues for this population into their age 60s and beyond
- **1971 FDA Drug Bulletin (November)** Diethylstilbestrol Contraindicated in Pregnancy
- **1972:** DES earns notoriety as the **first human transplacental carcinogen**
- **1976:** DES sons 4x greater prevalence of epididymal cysts & hypoplastic testes and semen disorders
- **1976:** Diethylstilbestrol in the Treatment of Rape Victims (Guidelines published)
- **1978 National Cancer Institute** published a report on DES after a federal task force investigates DES injuries
- **1982:** Adverse effects on the reproductive tract & reproductive performance in male/female offspring
- **1984:** Breast Cancer seen in DES Mothers given DES in pregnancy
- **1986:** Paraovarian cysts associated with prenatal DES exposure
- **1986:** First research focusing on mental health and psychiatric effects of prenatal DES exposure in daughters and sons

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- **1987:** Testicular tumors, epididymal cysts, retained hypotrophic testes and sperm abnormalities noted in DES Sons which a potential increased risk for developing carcinoma of the reproductive tract
- **1990:** Diethylstilbestrol, teratogenesis, and carcinogenesis: medical implications of its long-term sequelae, including third generation effects
- **1995:** Primary non-clear-cell adenocarcinomas of the vagina in older DES-exposed women
- **1996:** Diethylstilbestrol and risk of fatal breast cancer in a prospective cohort of US women
- **1999:** Dr. Arthur Herbst: Emphasizes there is no age limit for the development of clear cell cancer. DES daughters should be monitored past the age of 40.
- **2000:** Increased incidence of ectopic pregnancy, premature delivery, and miscarriage in DES daughters.
- **2001:** Long-term cancer risk in women given diethylstilbestrol (DES) during pregnancy
- **2002:** Hypospadias in sons of women exposed to diethylstilbestrol in utero
- **2004:** Estrogen treatment to reduce the adult height of tall girls: long-term effects on fertility
- **2004:** In utero exposures and the incidence of endometriosis
- **2007:** Preeclampsia risk in DES daughters documented
- **2008:** Research on 3rd generation DES granddaughters urges close surveillance for potential cancer risk
- **2009:** Further prevalence of male urogenital abnormalities is further recognized in DES sons
- **2009:** Unlocking the Mysteries of How DES Causes Harm: Epigenetic Mechanism HOXA10 gene
- **2010:** Birth Defects in the sons and daughters of women who were exposed in utero to diethylstilbestrol
- **2011:** Risk of psychiatric disorders in DES-exposed offspring is further documented
- **2013: Medical Conditions Among Adult Offspring Prenatally Exposed to Diethylstilbestrol** Analysis found a higher incidence of diabetes, cardiovascular disease, coronary artery disease, heart attack, high cholesterol, hypertension, osteoporosis, and bone fractures
- **2014:** Maternal exposure to DES during pregnancy and increased breast cancer risk in daughters
- **2015:** Research focuses on prenatal DES exposure in DES daughters and risk of obesity
- **2017:** Effect of In-Utero Exposure to High Dose Diethylstilbestrol on Intervertebral Disk
- **2017:** Prenatal diethylstilbestrol exposure and cancer risk in women –clear cell adenocarcinoma; breast cancer; pancreatic cancer
- **2017**: Cardiovascular risks doubled for diethylstilbestrol daughters: Increased risk for coronary artery disease and myocardial infarction
- **2017:** Risk of cervical intra-epithelial neoplasia and invasive cancer of the cervix in DES daughters
- **2018:** Epigenetic Risk for ADHD in Grandchildren of Diethylstilbestrol Users
- **2020:** Prenatal diethylstilbestrol exposure and risk of diabetes, gallbladder disease, and pancreatic disorders and malignancies
- **2023: NIH/NCI: Diethylstilbestrol (DES) Exposure and Cancer Guide Produced**

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Increased Risk for Breast Cancer in DES Mothers, DES Daughters, DES Granddaughters and Women exposed to DES (such as Morning After Pill, Dry up Breast Milk, Tall Girls)

Annual Mammograms for all DES-exposed females recommended from the NIH.

- **Monthly self-breast exams**
- **Annual breast screenings**
- **Yearly clinical breast exams**
- **Attention to breast health for DES Daughters and Granddaughters who report changes**

Breast Cancer Risk: 40 years of age or older substantially elevated

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Increased Risk for Vaginal and other Reproductive Cancers in DES Daughters and Women exposed to DES (such as Morning After Pill, Dry up Breast Milk, Tall Girls)

Specialized Annual GYN and Pap Smears

Cancer: Grade 2 or higher cervical intraepithelial neoplasia

● **Annual exams** should check for clear cell adenocarcinoma (CCA) of the vagina and/or cervix since DES Daughters are at a lifetime risk 40 times higher than unexposed

- Researchers are watching DES Granddaughters and recommend the same exam for DES Granddaughters.

● An important aspect of the special exam is palpation of the vagina to check for cancerous lumps under the surface especially in the Vagina

● For women that have had a hysterectomy or menopause, they should continue with this annual exam to screen for vaginal or cervical cancer.

Treatment Considerations:

● Cervical stenosis is a concern especially from cryosurgery and cone biopsy, researchers recommend caution

● LEEP procedure is used with the understanding the least invasive but diagnostically correct procedure is the goal

Specialized GYN exam should include the following per CDC Guidelines (2014)

- Clinical breast exam
- Vulvar inspection
- Vaginal and cervical inspection
  - – Inspection of epithelial surfaces of vagina
  - – Rotation of speculum to view anterior & posterior walls of vagina
- Cytology
  - – Separate specimens from vagina fornices and cervix: all specimens placed on one slide or in liquid media
- Palpation of vagina and cervix (an essential part of the exam)
  - – Palpate entire length of vagina, including fornices
  - – Note ridges or structural changes
- Bimanual rectal-vaginal exam
- Biopsy
  - – Areas of thickening or induration found during vaginal and cervical palpation
  - – Palpable nodules
  - – Discrete areas of varied colors or textures
  - – Atypical colposcopic findings
- Colposcopy
  - – If abnormal findings on Pap smear
- Iodine staining of vagina and cervix
  - – To confirm boundaries of epithelial changes
  - – Use Lugol's solution (half strength)
- Frequency of follow-up visits
  - – Determine on individual basis
  - – Focus on changes since initial evaluation — include the following: palpation, inspection, cervical & vaginal cytology
  - – Colposcopy, iodine staining, biopsy as needed
  - – Ask about interval bleeding or abnormal vaginal discharge

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DES Sons: Urological Concerns - Cryptorchidism, Epididymal cysts–Benign cysts, Hypospadias, Testicular Variocoeles, Infertility, Testicular Cancer Risk, Sexuality, Gender, & Psychiatric Effects

Recommended Annual Urological Exams

- **Monthly testicular self-exams**
- **Yearly exams by a physician (Urologist)**
- **Attention to male genitals for DES Sons & DES Grandsons who report changes**

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Increased Risk for Problem Pregnancies in DES Daughters and DES Granddaughters

Treat as High-Risk Pregnancies

- **Cumulative pregnancy risks** in women exposed to DES, as compared with those not exposed
- **Infertility**
- **Spontaneous Abortion**
- **Incompetent Cervix**
- **Preterm delivery**
- **Loss of second-trimester pregnancy**
- **Ectopic pregnancy**
- **Preeclampsia**
- **Stillbirth**

Patients pregnant with a history of DES exposure and/or a family history of DES exposure may need additional support during their pregnancy for these documented risk factors.

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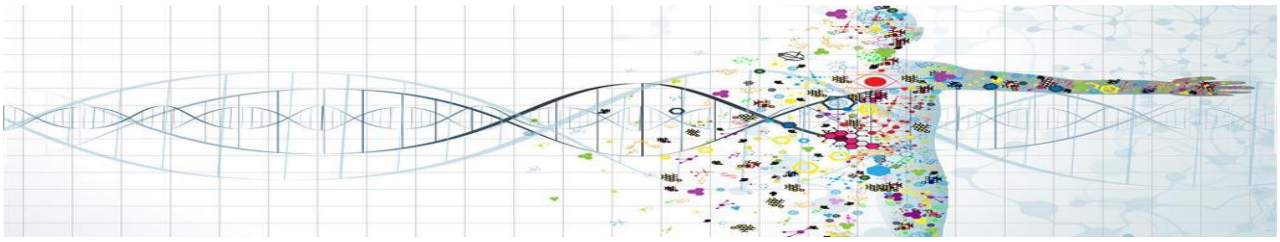

Increased Risk for Other Health Related Conditions in the DES Exposed

Research has noted other health related conditions in the DES Exposed

Annual Physical Exams and tests recommended by your physician
(Cardiac, CT scan, Lab work, Bone Density)

- **Cardiovascular disease**
  - Increased risk of high cholesterol
  - Hypertension
  - Coronary artery disease
  - Heart attack
- **Diabetes**
- **Pancreatic disorders**
- **Early menopause**
- **Osteoporosis**
- **Brittle Bones/Fractures**
- **Spinal degeneration**

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3rd Generation effects in DES Grandchildren

- **Ask your patients about a family history of DES Exposure**
- **DES Granddaughters need the same screening as DES Daughters**
- **DES Grandsons need the same screening as DES Sons**

Research has noted other health related conditions in the children and grandchildren of DES Exposed Sons and Daughters

Health related conditions to assess for in your patients

- Increased risk for neurodevelopmental effects, particularly ADHD
- Increased risk for psychiatric disorders including: psychosis, mood disorders, anxiety disorders, eating disorders, obsessive-compulsive disorders, violence and addictions
- Increased risk in DES granddaughters of irregular menses and amenorrhea
- Possible increase in infertility in DES granddaughters
- Increased risk of high cholesterol diagnosis in DES granddaughters
- Increased risk of preterm delivery and possibility of ectopic pregnancy in DES granddaughters
- Increased risk of genital tract anomalies in DES grandsons and granddaughters
- Increased risk of endometriosis in DES granddaughters

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DES and Psychiatric, Neurological, and Psychologic Effects

Research has noted other mental health and psychiatric conditions in DES-exposed populations.
Screen your patients for:

- **Depression and Anxiety**
- **ADHD**
- **Autism Spectrum Disorder**
- **Bipolar Disorder**
- **Mood and Sleep Disorders**
- **PTSD**
- **Eating Disorders**
- **Gender Identity Issues** *(see separate section at grad-mentor.com/research-des-sexuality)*

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DES Info Association & Diethylstilbestrol (DES) International Information and Research Group
DESInfo411@gmail.com *Karen Fernandes, R.N., CPHQ* DESExposed@gmail.com *Scott Kerlin, Ph. D*
Facebook: DES (Diethylstilbestrol) Info & DES Research and Support Group of Dr. Scott Kerlin