

Known Health Effects DES exposure in Males

1. Non-cancerous epididymal cysts (growths on the testicles);
2. Other genital abnormalities;
3. infertility

- My mother was prescribed DES while pregnant with me. Am I at an increased risk for any health problems?

Only a few studies have focused on health problems experienced by men exposed to DES before birth (in the womb), known as DES Sons. The research has focused on the following health concerns among DES Sons.

Non-Cancerous Epididymal Cysts

The most consistent research finding for DES Sons indicates that they have an increased risk for non-cancerous epididymal cysts, which are growths on the testicles (Bibbo, 1977; Gill, 1979; Conley, 1983; Niculescu, 1985; Wilcox, 1995). In one study, 21% of DES Sons had non-cancerous epididymal cysts compared with 5% of unexposed men (Gill, 1979).

Other Genital Abnormalities

Whether DES increases the risk for other genital abnormalities in men remains unclear. A few studies have reported that DES Sons experience a greater likelihood of being born with

- a) undescended testicles (cryptorchidism),
- b) a misplaced opening of the penis (hypospadias), or
- c) a smaller than normal penis (microphallus).

These studies estimated that 15%-32% of DES Sons experience one or more of these structural differences compared with 5%-8% of unexposed men (Gill, 1979; Wilcox, 1995). Other studies, however, have not identified an increased risk of structural differences (Leary, 1984; Vessey, 1983). Because findings have been inconsistent, researchers cannot say with certainty that DES causes these types of genital abnormalities in DES-exposed men.

Infertility

DES Sons are not at an increased risk for infertility. Some DES Sons have been concerned that DES exposure might be linked to infertility. Although one study found a lower sperm count in men exposed to DES compared with unexposed men (Gill, 1979), a 40-year follow-up study of DES Sons found no increased risk of infertility among men exposed to DES before birth (Wilcox, 1995).

Men Exposed to DES before Birth (in the Womb), Known as DES Sons

1. Ambramsson L. On the investigation of men from infertile relations: a clinical study with special regard to anamnesis, physical examination, semen-, hormone- and chromosome analyses, from men with non-"normal" semen. *Scand J Urol Nephrol* 1988;Suppl 113:1-47.
2. Ambramsson L, Duchek M, Lundgren B. Conception rate for infertile couples: the importance of anamnesis and signs of genital disease in men with abnormal semen findings. *Scand J Urol Nephrol* 1989;23(3):165-71.
3. Andonian RW, Kessler R. Transplacental exposure to diethylstilbestrol in men. *Urology* 1979;13:276.
4. Bibbo M, Al-Naqeeb M, Baccarini I, Gill W, Newton M, Sleeper KM, et al. Follow-up study of male and female offspring of DES-treated mothers: a preliminary report. *J Reprod Med* 1975;15:29.
5. Bibbo M, Gill WB, Azizi F, Blough R, Fang VS, Rosenfield RL, et al. Follow-up study of male and female offspring of DES-exposed mothers. *Obstet Gynecol* 1977;49(1):1-7.
6. Bibbo M, Ali I, Al-Naqeeb M, Baccarini I, Climaco LA, Gill W, et al. Cytologic findings in female and male offspring of DES-treated mothers. *Acta Cytol* 1975;19:568.
7. Braun MM, Ahlbom A, Floderus B, Brinton LA, Hoover RN. Effect of twinship on incidence of cancer of the testis, breast, and other sites [Sweden]. *Cancer Causes Control* 1995;6:519-24.
8. Brown LM, Pottern LM, Hoover RN. Prenatal and perinatal risk factors for testicular cancer. *Cancer Res* 1986;46:4812-6.
9. Clark LC, Portier KM. Diethylstilbestrol and the risk of cancer. *N Eng J Med* 1979;300(5):263-4.
10. Conley GR, Sant GR, Ucci AA, Micheson HD. Seminoma and epididymal cysts in a young man with known diethylstilbestrol exposure in utero. *JAMA* 1983;249:1325-6.
11. Cosgrove MD, Benton B, Henderson BE. Male genitourinary abnormalities and maternal diethylstilbestrol. *J Urol* 1977;117(2):220-2.
12. Depue RH, Pike MC, Henderson BE. Estrogen exposure during gestation and risk of testicular cancer. *J Natl Cancer Inst* 1983;71:1151-5.
13. Driscoll SG, Taylor SH. Effects of prenatal maternal estrogen on the male urogenital tract. *Obstet Gynecol* 1980;56(5):537-42.

14. Gershman ST, Stolley PD. A case-control study of testicular cancer using Connecticut Tumor Registry data. *Int J Epidemiol* 1988;17:738-42.
15. Gill WB, Schumacher GFB, Bibbo M, Straus FH, Schoenberg HW. Association of diethylstilbestrol exposure in utero with cryptorchidism, testicular hypoplasia and semen abnormalities. *J Urol* 1979;122:36-9.
16. Gill WB, Schumacher GFB, Bibbo M. Structural and functional abnormalities in the sex organs of male offspring of mothers treated with diethylstilbestrol (DES). *J Reprod Med* 1976;16(4):147-53.
17. Gill WB, Schumacher GFB, Bibbo M. Pathological semen and anatomical abnormalities of the genital tract in human male subjects exposed to diethylstilbestrol in utero. *J Urol* 1977;117:477-80.
18. Gill WB, Schumacher GFB, Hubby MM, et al. Male genital tract changes in humans following intrauterine exposure to diethylstilbestrol [review]. In: Herbst AL, Bern HA, editors. *Developmental effects of diethylstilbestrol (DES) in pregnancy*. New York: Thieme-Stratton, Inc.; 1981. Chapter 8.
19. Goldberg J, Falcone T. Effect of diethylstilbestrol on reproductive function. *Fertil Steril* 1999;72:1-7.
20. Goy RB, McEwen BS. *Sexual differentiation of the brain*. Cambridge (MA): The MIT Press; 1980.
21. Herbst AL. Diethylstilbestrol and other sex hormones during pregnancy [review]. *Obstet Gynecol* 1981;58(Suppl):S35-S40.
22. Hembree WC, Nagler HM, Fang JS, Myles EL, Jagiello GM. Infertility in a patient with abnormal spermatogenesis and in utero DES exposure [case report]. *Int J Fert* 1988;33(3):173-7.
23. Henderson BE, Benton B, Jing J, Yu MC, Pike MC. Risk factors for cancer of the testis in young men. *Int J Cancer* 1979;23:598-602.
24. Henderson BE, Benton B, Cosgrove M, Baptista J, Aldrich J, Townsend D. Urogenital tract abnormalities in sons of women treated with diethylstilbestrol. *Pediatrics* 1976;58(4):505-7.
25. Hinman F Jr. Unilateral abdominal cryptorchidism. *J Urol* 1979;122:71-5.
26. Kappel B, Hansen K, Moller J, Faaborg-Andersen J. Human placental lactogen and dU-estrogen levels in normal twin pregnancies. *Acta Genet Med Gemellol (Roma)* 1985;34:59-65.
27. Leary FJ, Resseguie LJ, Kurland LT, O'Brien PC, Emslander RF, Noller K. Males exposed in utero to diethylstilbestrol. *JAMA* 1984;255(21):2984-9.
28. Loughlin JE, Robboy SJ, Morrison AS. Risk factors for cancer of the testis [letter to the editor]. *N Engl J Med* 1980;303(2):112-3.
29. McLachlan JA, Newbold RR, Li S, Negishi M. Are estrogens carcinogenic during development of the testes? *APMIS* 1998;106(1):240-4.

30. McLachlan JA. Rodent models for perinatal exposure to diethylstilbestrol and their relation to human disease in the male. In: Herbst AL, Bern HA, editors. Developmental effects of diethylstilbestrol (DES) in pregnancy. New York: Thieme-Stratton, Inc.; 1981.
31. McLachlan et al. Science. 1975;190:991-2.
32. Moller H, Skakkebaek NE. Testicular cancer and cryptorchidism in relation to prenatal factors: case-control studies in Denmark. Cancer Causes Control. 1997;8:904-12.
33. Moss A, Osmond D, Bacchetti P, Torit FM, Gurgin V. Hormonal risk factors in testicular cancer: a case-control study. Am J Epidemiol 1986;124:39-52.
34. Newbold RR, Bullock BC, McLachlan JA. Lesions of the rete testis in mice exposed prenatally to diethylstilbestrol. Cancer Res 1985;45:5145-8.
35. Newbold RR, Bullock BC, McLachlan JA. Testicular tumors in mice exposed in utero to diethylstilbestrol. J Urol 1987;138:1446-50.
36. Niculescu A. Effects of in utero exposure to DES on male progeny. J Obstet Gynecol Neonatal Nurs 1985;14:468-70.
37. Panagiotopoulou K, Katsouyanni K, Petridou E, Garas Y, Tzonou A, Trichopoulos D. Maternal age, parity, and pregnancy estrogens. Cancer Causes Control 1990;11:119-24.
38. Petridou E, Roukas K, Dessypris N, Aravantinos G, Bafaloukos D, Efraimidis A, et al. Baldness and other correlates of sex hormones in relation to testicular cancer. Int J Cancer 1997;71:982-5.
39. Pylkkanen L, Makela S, Valve E, Harkonen P, Toikkanen S, Santti R. Prostatic dysplasia associated with increased expression of c-myc in neonatally estrogenized mice. J Urol 1993;149:1593-1601.
40. Rosing U, Carlstrom K. Serum levels of unconjugated and total oestrogens and dehydroepiandrosterone, progesterone and urinary oestriol excretion in pre-eclampsia. Gynecol Obstet Invest 1984;18:199-205.
41. Schottenfeld D, Warschauer ME, Sherlock S, Zauber AG, Leder M, Payne R. The epidemiology of testicular cancer in young adults. Am J Epidemiol 1980;112:232-46.
42. Seigler AM, Wang CF, Friberg J. Fertility of diethylstilbestrol exposed offspring [review]. Fertil Steril 1979;31:601-7.
43. Stenchever MA, Williamson RA, Leonard J, Karp LE, Ley B, Shy K, et al. Possible relationship between in utero diethylstilbestrol (DES) exposure and male infertility. Am J Obstet Gynecol 1981;140:186-93.
44. Stillman RJ. In utero exposure to diethylstilbestrol: adverse effects on the reproductive tract and reproductive performance in male and female offspring [review]. Am J Obstet Gynecol 1982;142:905-21.

45. Strohsnitter WC, Noller KL, Hoover RN, Robboy SJ, Palmer JR, Titus-Ernstoff L, et al. Cancer risk in men exposed in utero to diethylstilbestrol. *J Natl Cancer Inst* 2001;93(7):545-51.
46. Turusov VS, Trukhanova LS, Parfenov YD, Tomatis L. Occurrence of tumors in the descendants of CBA male mice prenatally treated with diethylstilbestrol. *Int J Cancer* 1992; 50:131-5.
47. Vessey MP, Fairweather DVI, Norman-Smith B, Buckley J. A randomized double-blind controlled trial of the value of diethylstilbestrol therapy in pregnancy: long-term follow-up of mothers and their offspring. *Br J Obstet Gynaecol* 1983;90:1007-17.
48. Vessey MP. Epidemiologic studies of the effects of diethylstilbestrol [review]. *IARC Sci Publ* 1989;96:335-48.
49. Whitehead ED, Leiter E. Genital abnormalities and abnormal semen analyses in males exposed to diethylstilbestrol (DES) in utero. *J Urol* 1981;125:47-50.
50. Wilcox AJ, Baird DD, Weinberg CR, Hornsby PP, Herbst AL. Fertility in men exposed prenatally to diethylstilbestrol. *N Engl J Med* 1995;332:1411-6.
51. Wingard DL, Turiel J. Long-term effects of exposure to diethylstilbestrol. *West J Med* 1988;149(5):551-4.