Gender-related Behavior in Women Exposed Prenatally to Diethylstilbestrol

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Accumulating evidence in experimental animals over the past three decades suggests that mammalian brain development and differentiation of the central nervous system are influenced by perinatal exposure to sex hormones. Hence, changes in human behavioral patterns may be associated with prenatal exposure to estrogenic substances such as diethylstilbestrol (DES). This paper reviews relevant studies from a series of laboratories and finds that no clear-cut differences can be demonstrated to date between unexposed and DES-exposed women in gender-related behavior, although the physical and psychological impact of the problems associated with exposure to DES are well documented. If both prenatal and postnatal influences such as social, economic, and environmental factors are taken into consideration, individual variation is more apparent than differences in gender-related behavior between unexposed and DES-exposed women. In summary, gender-related behavior is determined by a complex array of interacting factors, and prenatal influences are only one of many developmental events. More studies are needed using larger populations with carefully controlled selection criteria to suggest a direct role of prenatal DES exposure on subsequent gender-related behavior. *Key words*: Developmental imprinting, diethylstilbestrol, environmental estrogens, gender-related behavior, perinatal exposure to sex hormones. *Environ Health Perspect* 101: 208–213(1993)

Diethylstilbestrol (DES), a synthetic estrogen, was first synthesized in 1938 by Sir Edward Charles Dodds (*1*). Thereafter, for almost three decades, DES was used as a therapeutic agent for the prevention of pregnancy complications and threatened miscarriage. Although the full extent of DES use remains unknown, it has been estimated that as few as 500,000 or as many as 4 million pregnant women were treated with DES (*2,3*). In the early 1970s, the *New England Journal of Medicine* published an article that reported the occurrence of a rare form of cancer of the reproductive tract in daughters of women who received DES during pregnancy (*4,5*). Subsequent studies reported that although the risk of cancer is estimated to be small (*6*) and in the order of 1 per 1000 of the exposed individuals (*7*), various other health problems are quite common. Anatomical changes in the reproductive tract (*8–10*), increased risks of menstrual irregularities (*11*), and a poorer prognosis for pregnancy outcome (*12–16*) are prevalent. For a review of the various aspects of the DES problem, see Herbst and Bern (*17*), Orenberg (*18*), and Edelman (*3*).

Altered reproductive tract development caused by treating rodents with DES or other estrogenic substances during fetal life has been the subject of extensive research and has led to the development of an experimental model to investigate the anatomical anomalies associated with intrauterine exposure to DES (*19*). Studies have documented that DES treatment of mice during development results in similar abnormalities as those reported in women (*19–21*). In fact, this experimental mouse model has been useful as a predictor of abnormalities in the oviduct as well as decreased pregnancy outcome in the human population (*22–27*). Although prenatal DES treatment is no longer an accepted medical practice, many other hormones and chemicals entering our environment every year may have estrogenic activity and therefore pose similar problems to those caused by DES (*28*).

Evidence in experimental animals has suggested that mammalian brain development and differentiation of the central nervous system is influenced by perinatal exposure to sex hormones. Rodent models have been used extensively in these studies. Administration of estrogens, including estradiol and DES, has a masculinizing effect on some aspects of sexual behavior in female rats, and a demasculinizing effect on the behavior of male rats if exposure occurs during critical stages of development (*29,30*). This seemingly paradoxical effect of estrogens in rodents has been explained by the fact that estradiol is a metabolite of testosterone, and estrogen is thought to act at the cellular level to masculinize many aspects of behavioral and neural development (*31*). The developing female rodent is protected from the influences of maternal or ovarian estrogens by an estrogen-binding factor called α-fetoprotein (AFP), which normally binds and prevents estrogens that circulate in the feto-placental system from reaching the brain, thus rendering them biologically inactive (*32*). The developing male rodent is also protected from maternal estrogen by AFP; however, testosterone produced by the fetal testes enters the brain, is metabolized to estrogen at the intracellular level, and thereby results in neural and behavioral masculinization (*32*). DES, a nonsteroidal estrogenic compound, bypasses these protective mechanisms due to its lack of binding activity with AFP, therefore having effects on the differentiating brain similar to that of androgens that are converted to estrogens under normal conditions of development. Thus, the behavior of female animals exposed to DES would be more similar to the behavior of males than to unexposed females. Support for this theory can be found in numerous reports (*33–35*).

Animal studies have also shown that prenatal or perinatal DES alters features of sex-dimorphic juvenile social play in female rats (*36*) and increases masculine mounting behavior while decreasing feminine lordosis in adult, female guinea pigs (*37*). Subsequent studies describe the effect of developmental exposure to estrogenic compounds on sex-related reproductive traits (*38*). DES has also been reported to cause structural changes such as an increase in the sexually dimorphic nucleus of the preoptic area of the brain of experimental animals including rats and guinea pigs (*39–41*).

Data on the effects of perinatal exposure to estrogens in nonhuman primates is scant. Slikker et al. (*42*) reported that in rhesus monkeys substantial amounts of DES reach the fetal compartment unaltered, which is in contrast to estradiol. Of greater interest is the study by Fuller et al. (*43*) that showed a lasting effect of prenatal DES exposure on gonadotropin patterns of infant rhesus monkeys; this is one of the first studies suggesting direct organizational effects of prenatal DES on sexually dimorphic areas of the primate brain. Although this area of research has been the

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subject of much study, data remain inconclusive in regard to a relationship of these structural alterations with subsequent behavioral modifications.

The generalization of animal behavior to humans, in particular in relation to sexual orientation, is controversial (*44–48*). However, considering the voluminous amounts of experimental animal data, potential human behavioral abnormalities should be examined in addition to the well-documented anatomical alterations in the reproductive tract of women exposed to DES prenatally. Recent studies describing sexual dimorphism in the organization of specific regions in the human brain (*49–54*) point to the fact that hormones play an important role in the structural development and differentiation of the brain. This report reviews relevant clinical and basic science studies from a series of laboratories to evaluate the present status of gender-related behavioral patterns reported in DES-exposed women and to determine if further studies are warranted to predict possible changes in the human population.

To evaluate the current status of gender-related behavioral traits in prenatally DES-exposed women, I undertook an extensive computer search of the existing literature. Detailed descriptions of these searches are as follows:

1) Psychinfo, File 11 (Psychological Abstracts Information Service, Arlington, Virginia), a database that covers the world's literature in psychology and related behavioral and social sciences, was searched back to 1967. For this database, I searched the terms "human" and "diethylstilbestrol" (including all synonyms, i.e., DES, stilbestrol, estrogens, sex hormones) with the following categories: prenatal development, sexual development, biosexuality, psychosexual development, drug-induced congenital disorder, and gender identity. Although this database scanned more than 950 periodicals, technical reports, and monographs for each year, only 17 articles were identified, 9 of which were relevant to this project because they described gender-related behavior traits in women who were prenatally exposed to DES.

2) Medline, the National Library of Medicine's bibliographic database, which covers the fields of medicine, nursing, dentistry, veterinary medicine, and the preclinical sciences, was researched back to 1966. For the last 2 years, Medline has contained between 300,000 and 500,000 citations. Previous years include a total of about 6 million records in backfile. Using the terms "diethylstilbestrol" (DES) or "estrogens" with terms such as "psychosocial factors," "psychosocial development," "human sex differences," and "gender identity," no additional relevant articles were located that were not identified in the Psychinfo search. I found five articles describing the emotional impact of DES exposure, but excluded them from evaluation because gender-related behavior was not specifically described.

3) The references cited in all reports identified by Psychinfo and Medline, including those reports that were excluded for lack of relevance to this study, were scanned by title to identify any additional studies describing gender-related behavior in DES-exposed women. Also, I scanned referenced articles by author; any contribution by A.A. Ehrhardt, H.F. Meyer-Bahlburg, E.J. Saunders, M.M. Hines, and R.W. Goy were examined because these authors were associated with current (1976 to present) published reports in the field. Using this approach I located one additional review article by Ehrhardt and Meyer-Bahlburg, but this report did not specifically study DES exposure. Two additional relevant articles by M. Hines and A.A. Ehrhardt were located by the author search scan.

4) For additional background data, I used a less systematic approach to identify articles describing the effects of estrogenic and androgenic hormones on the sexual differentiation of the brain in experimental animals. I examined 17 articles including 3 extensive review articles. All 17 articles were published after 1980.

After reviewing the literature identified by computer search, which described gender-related behavior patterns reported in prenatally DES-exposed women, I found seven articles that described a difference in behavior in DES-exposed individuals as compared to unexposed individuals. Six of the articles described behavior traits that tended to be more masculine in the DES-exposed population (*54–59*), and one article described behavior traits that tended to be more feminine than the corresponding control population (*60*). Each report described at least one altered behavior pattern, but no specific trait was identified that was similar among the reports.

All seven reports identified more behavior trait similarities between DES-exposed women and unexposed women than differences. The findings of more similarities in behavior between control and DES-exposed groups is even more striking considering the bias of the studies: these reports were characterized by an assumption that there would be differences between groups, and the experimental protocols were specifically designed to test for differences, not similarities. The results of these articles are summarized in Table 1. In all of these studies, the measurements of "masculine" or "feminine" behavior refer to behavior that is more typical for boys or girls rather than exclusively male or female.

The earliest article I reviewed (*54*) was a doctoral dissertation that described increased brain lateralization in women that were prenatally exposed to DES as compared to their unexposed sisters. This study consisted of 25 women who had been exposed prenatally to DES matched with 25 of their unexposed sisters. All women came from higher socioeconomic groups. In the DES-exposed group, increased brain lateralization was demonstrated using auditory and visual stimuli. Cerebral lateralization, or specialization of the two hemispheres of the brain for different types of cognitive processing, was described in a review by McGlone (*53*) and reported to differ in men and women; men tend to show a greater left-hemisphere specialization for verbal stimuli than women, and McGlone suggested that this difference might cause sex differences in cognitive abilities.

In contrast to the differences reported in brain lateralization, DES-exposed women and their unexposed sisters did not differ significantly in the performance of other tested behaviors such as athletic activity, career interests, marriage, motherhood, smoking, academic attainment, sexually dimorphic personality characteristics (dominance, arousability, and pleasure), and sexually dimorphic cognitive abilities (visuospatial ability, verbal ability, and clerical skills). Hines (*54*) suggested that the lack of a relationship between DES exposure and these sexually dimorphic behaviors might be due to "insufficiently sensitive dependent measures." An assumption was made that because brain lateralization was different, behavioral traits should also be different and could be demonstrated if the tests were sufficiently sensitive. Because no significant differences could be demonstrated, an explanation was offered that activational hormone effects were not considered in the study. The author's conclusion to this study, based on one altered parameter, was that human sexual differentiation, like sexual differentiation in other mammals, is influenced by prenatal hormone levels, including estrogens. The discussion and conclusions presented in this 1981 paper as well as a follow-up paper in 1982 (*55*) reflected the general opinion in the early part of the decade that prenatal hormones influence adult gender identity and sexual behavior.

Hines and Shipley (*56*) continued to study behavioral traits in women prenatally exposed to DES. As in earlier reports, the DES-exposed women demonstrated a more masculine pattern of brain lateralization than did their sisters on verbal dichotic tasks. However, no differences

Table 1. Comparison of unexposed and prenatally DES-exposed women

Trait studied[a]	Result	Reference[b]
Childhood play	Less in DES-exposed	(57)
	No difference	(59)
Rough and tumble play	Less in DES-exposed	(57)
	No significant difference	(59)
Interest in cosmetics and hair	More feminine after DES exposure	(60)
Physically energetic play	No difference	(57)
Aggression	No difference	(65)
Athletic activity	No difference	(54)
	No difference	(59)
Smoking	No difference but too few to evaluate	(54)
Interest in hobbies and pets	Less in DES exposed	(65)
Social relation problems	More in DES exposed	(65)
Frequency of social contacts and closeness of family ties	No difference	(65)
Interest in motherhood and child care	No difference but too few to evaluate	(54)
	More feminine in DES exposed	(60)
	Less maternal interest in DES exposed	(57)
	Less orientation toward parenting	(59)
	No difference	(66)
Interest in marriage	No difference but too few to evaluate	(54)
	Less of interest in DES exposed	(61)
	Less of interest in DES exposed	(57)
Academic attainment (GPA)	No significant difference	(54)
Career interests and college major	No significant difference	(54)
	More feminine in DES exposed	(60)
Sexually dimorphic personality characteristics (i.e., dominance, arousability, pleasure)	No significant difference	(54)
Maturity (onset of menstruation)	No difference	(56)
Various other phycho-sexual milestones	No difference	(61)
Disorders of sexual desire	Higher in DES exposed	(58)
Hyposexuality	Higher in DES exposed	(58)
Bi- or homosexuality	Higher in DES exposed	(58)
Cognitive abilities		
Visuospatial ability	No difference	(54)
	No difference	(56)
Verbal ability	No significant difference	(54)
	No significant difference	(56)
Clerical skills (means adjusted for birth order)	No difference	(54)
Overall intellectual ability	No difference	(56)
Patterns of cerebral lateralization	More in DES exposed	(54)
	More in DES exposed	(56)

[a]The references are organized by year and similar traits to demonstrate prevailing theories of gender-related behavior and how the ideas change over time.
[b]The measurements of masculine and feminine behavior almost always reveal a distribution that is represented by widely overlapping curves rather than being totally dichotomous. Thus, "masculine" or "feminine" behavior refers to behavior that is more typical for boys or girls rather than exclusive for male or female.

were seen between DES-exposed and unexposed women in verbal or visuospatial abilities. Physical indexes such as height, weight, and onset of menstruation were similar across groups. The conclusion drawn in the follow-up report stated that "it is important to note that the lateralization differences observed between DES-exposed women and their unexposed sisters, like those observed between men and women in general, although statistically significant, are small and do not suggest any sort of abnormality" (*56*: 91). In addition, Hines and Shipley pointed out that normal intellectual and physical development were not altered in the DES-exposed women, so there was no reason to expect impared function on the basis of their findings.

Another study was published in 1984 describing a group of 30 women 17–30 years old with a confirmed record of prenatal exposure to DES. These women were compared to 30 women of similar age and demographic background with a history of abnormal Pap smear findings but no DES exposure. Unlike the Hines studies (*54–56*), which were conducted in DES screening clinics at the University of California-Los Angeles and Stanford University Medical Center, the Meyer-Bahlburg study was carried out at the DES screening clinic at Brookdale Hospital Medical Center, Brooklyn, New York. The researchers concluded from their study that the DES-exposed and unexposed women did not differ in age at menarche or in age at attainment of various psychosexual milestones. The authors stated that their data contrasted with the effects reported for DES and other estrogens in lower mammals, but suggested that the differences could be explained by the fact that in humans, postnatal rather than prenatal hormone history influences the timing of puberty. They also stated that their findings suggested no effect of prenatal DES exposure in psychosexual milestones in adolescent women; this was in contrast to the findings of other investigators on human males with similar DES exposure (*62,63*). The conclusion of the Meyer-Bahlburg report was that the influence of prenatal hormones on the timing of puberty and/or adolescent psychosexual milestones had not been conclusively demonstrated in humans.

Ehrhardt et al. published a report in 1984 (*60*) that was designed to answer the following questions: Does prenatal exposure to various hormone therapies have discernible side effects on sex-dimorphic behavior in childhood? Does the direction of these effects agree with data provided by animal research? In this double-blind study, both boys and girls were described, but here I focus only on the data for females. In the female sample, only 15 DES-exposed subjects were identified, and 10 of these women had been prenatally exposed to additional thyroid hormone therapy. Fifteen closely matched control subjects were also identified. The children ranged in age from 8 to 12 years and the control group was slightly older. All subjects were Caucasian and typically from middle-class families. The DES group had been exposed during gestation to sex hormones for varied times ranging from 1 to 41 weeks. Children were excluded from the study if they had any congenital abnormalities at birth. Whether this group of DES-exposed women differed from the experimental subjects reported by Meyer-Bahlburg et al. (*61*) in 1984 was not apparent. The findings described by Erhardt et al. were in contrast to all other published reports, which suggested a trend

toward more masculine behavior. Ehrhardt et al. described more stereotypically feminine behavior in almost all of the parameters examined in the DES-exposed women (*60*). Aggressive behavior was the only trait tested that showed no difference between the DES-exposed women and the control group. The authors concluded that prenatal sex hormone treatment was associated with an effect on sex-dimorphic behavior in women with a trend toward increased stereotypic femininity.

In 1985, Ehrhardt et al. described 30 women 17–30 years old with documented prenatal exposure to DES (*57*). These women were compared with 30 women from the same medical clinic with similar demographic characteristics who had a history of abnormal Pap smears (*57*). Some of the DES-exposed women were also compared with their unexposed sisters. Although it is not clear, the subjects may have represented a subset of women that were described in earlier studies (*60,61*), as the testing occurred at the DES-screening clinic in Brookdale Hospital Medical Center, Brooklyn, New York, as before. The significant findings of increased bisexuality and homosexuality in the DES-exposed women was in marked contrast to these author's previous findings of increased femininity (*60*), although the subjects were older than those reported in previous studies. The authors concluded that their findings could be considered suggestive but were not to be taken as proof of a hormonal contribution to the development of sexual orientation in humans.

A major problem in the design of the Ehrhardt et al. (*57*) study is that women with abnormal Pap smears are usually more sexually active and have a greater number of sexual partners than women who do not have intraepithelial disease of the cervix. Thus, to suggest that the DES-exposed women had an increased frequency of bisexuality and homosexuality as compared to a group of women who were known to be more heterosexually active is inaccurate. Furthermore, even if hormones in general, and DES in particular, do have some influence on the development of sexual orientation, 75% of the DES-exposed women in this study were exclusively heterosexual in spite of DES exposure; only 1 woman out of 30 in this study was nearly exclusively homosexual. Therefore, the data presented in this report seem to suggest little if any DES effects on sexual orientation despite statements in the abstract of the paper suggesting otherwise (*57*).

Apparently the same group of 30 DES-exposed women and corresponding 30 unexposed women were followed by Meyer-Bahlburg et al. (*58*). The DES-exposed women had less well-established sex-partner relationships, less experience with childbearing, and lower sexual desire and enjoyment, sexual excitability, and orgasmic coital functioning, although they were comparable to the unexposed women with regard to such sexual dysfunctions as vaginismus and dyspareunia. The authors thought that the sex-behavior differences were probably underestimates because three of the DES subjects refused to answer a number of intimate sexual questions. The studies were conducted by interviewers who were familiar with the historical background of the subjects. Meyer-Bahlburg et al. described several possible contributing factors other than prenatal hormone treatment to explain their findings of behavioral alterations. These explanations were based on lack of interrater reliability, interview variables, differences in sexual partners of the tested cohort, differences in reproductive status and religious affiliation, differences in psychological status such as depression, the fact the sample group was physician-referred, and the awareness of the genital effects and of the general health and reproductive risks of DES exposure, which might inhibit sexuality. Despite these variables, the authors compared their findings of bisexuality and homosexuality in the DES-exposed women to data obtained from animal studies (*58*). Finally, the possibility of estrogen-induced lesions of the brain (similar to animal studies) was suggested, but the authors recommended additional DES samples with more detailed prenatal treatment information. In summary, Meyer-Bahlburg and co-workers concluded that the findings of abnormal sexual orientation in the DES-exposed women was preliminary and that these findings needed to be replicated in other study groups, which has not been accomplished to date.

Ehrhardt reported other sexually dimorphic traits in DES-exposed women in 1984 at a Nebraska Symposium on Motivation (*64*). For several years, both she and Meyer-Bahlburg had been following several groups of DES-treated females and males with different control groups, some matched on health conditions, others on family status (i.e., unexposed siblings). One of their earlier analyses suggested DES females were less feminine and more masculine than controls (*57*). The data presented at the symposium indicated some support for their earlier findings: DES females showed less parenting rehearsal in childhood; that is, less doll play, less maternal role playing, less interest in infants. They also showed less interest in getting married and were less inclined to marry and attempt pregnancy in adulthood. There was no difference between the two groups in physically energetic play behavior. In fact, according to their mothers, DES females were less frequently involved in rough-and-tumble play during childhood (*60*). As Ehrhardt cautioned (*64*), other postnatal factors need to be considered. For example, awareness of reproductive difficulties in adulthood may have led to less interest in parenting in the DES women. Ehrhardt set the stage for the evolving opinions of specific influences on gender-related behavior in the mid-1980s: she stated that "the study of gender-related behavior has been hampered in the past by the narrowly defined main-effect model that posits biology versus learning" (*64*: 54). In contrast, Ehrhardt suggested a broader biosocial perspective that includes "constitutional as well as environmental factors" in understanding complex phenomena such as gender identity development and other aspects of gender-related behavior. In summary, she suggests using an interactional model (*64*). Her approach represents an understanding of the problems faced by clinicians and basic scientists in the 1980s.

In 1987, Ehrhardt and co-workers (*65*) published a report on the long-term effects of prenatal exposure to DES on overall psychologic functioning in females. The 30 DES-exposed women (17–30 years old) and the 30 control women may have been the same cohort described in earlier studies by these investigators. The DES women reported slightly more depressive episodes than the control group and significantly more problems in social relations with spouses and other significant persons. Other gender-related behavior differences described in the DES women suggested less interest in hobbies and pets as compared to corresponding controls. Because the sample size was small in this study and the data were preliminary, no definitive differences in gender-related behavior were established in the DES-exposed women.

Another study was conducted in 1989 by Ehrhardt et al. (*59*). The data from this study suggested that DES-exposed women showed less orientation toward parenting than the controls. There were no consistent group differences in other gender-role behaviors (*59*). It is interesting to note that bisexuality and homosexuality had been reported earlier in one of their DES-exposed groups (*57*); if this was the same sample, the possibility exists that there was a change in the group as they aged. However, Ehrhardt et al. concluded that prenatal DES has effects on human sex-dimorphic behavior, although they suggested caution in interpreting the data because of the potential confounding variables associated with the study.

Finally, in their most recent study, Lish et al. (*66*) failed to replicate the findings of decreased interest in parenting described in their earlier reports (*59*). Although they studied a different sample, similar methodology was used. These authors stated that the assessment devices used in their current study would have certainly detected masculinization in the DES-exposed women if it were present.

Surprisingly, there have been few studies conducted with humans to evaluate the behavioral effects resulting from *in utero* exposure to DES or other sex hormones. Of the studies reported, varied experimental designs or procedures were used to evaluate the test groups. Overall, the published studies to date do not offer definitive evaluations of DES-exposed women because most did not evaluate enough subjects; some studies did not include a control group or used inappropriate control groups; the DES groups were composed of women that had been exposed for various times and doses during gestation; and some studies did not evaluate the effects of DES *in utero* exposure specifically, but rather considered the effects of estrogens, progestins, and a combination of the two compounds (*67,68*).

There were other major limitations of these studies. Most were based on evaluations of subjects ranked by their performance on psychological tests and not on their actual behavioral patterns in nonlaboratory environments. The results from some of these studies carried out in laboratory settings suggested that *in utero* exposure to DES may induce behavioral changes, but they did not indicate whether the measured behavioral patterns were "abnormal" or were within an accepted "normal" range. It is important to note that of the studies describing childhood and adolescent behavior, only subtle behavioral changes were mentioned; no socially unacceptable or deviant behavior has been associated with early DES hormone exposure.

Although there is ample evidence from studies using laboratory animals that prenatal exposure to sex hormones may affect behavior, over the last few years serious objections have been raised when animal behaviors are generalized to human behaviors (*44–48*). The conclusion has been that if it is important to understand human behavior, human beings should be studied; using animal data to generalize and cover human behavior is simply not appropriate. This is not only because humans possess unique characteristics that make their behavior qualitatively different but also because factors as variable and complex as social behavior and gender-related behavior patterns must be studied separately in every species. Considering all the data accumulated about the development of social behavior in a large number of species, and in particular, the major differences that exist both within and between them, it should be clear that sound generalizations covering many or even all animal species are few and far between. Social behavior is not a single or simple thing, and it is not the outcome of a simple developmental process in all animals, or even in primates. This is not to say that animal studies are not important, but care must be exercised in extrapolating data using animal studies.

Research on the relationships between prenatal exposure to sex hormones and the subsequent behavioral patterns of the exposed offspring is still a relatively new field. Recent studies suggest a wide variation in behavioral responses among species, as well as more similarities than differences between females and males of the same species. Perhaps more sensitive testing methods are making these comparisons more valid than in the past. Also, investigators are becoming more open-minded with their approach in designing experiments. Perhaps the concepts of what constitutes masculine or feminine behavior are more flexible. In addition, authors often acknowledge that many factors, including prenatal environment, play a substantial role in subsequent brain development and neuroendocrine differentiation as well as behavioral traits. The idea of interactive developmental forces has become more widely accepted.

It is apparent that additional basic research on the effects of estrogens in the developing brain, as well as more experimental and observational studies to evaluate the effects of *in utero* exposure to estrogens, is needed. However, caution should be taken in extrapolating animal behavior to humans. At present, no definitive conclusion can be reached regarding the effects of DES or other sex hormones on the development of gender-specific behaviors in children, adolescents, or adults.

Summary

This review has focused on gender-related behavior, a field in which accumulating evidence suggests that both prenatal and postnatal influences have a significant effect. Considering all the prenatal factors, estrogens such as DES are of particular interest in studying the development of gender-related behaviors. However, there are a vast number of biological and psychosocial factors that are interacting to explain specific behavioral traits. To date, no clear-cut differences have been reported between unexposed and DES-exposed women in gender-related behavior. If both prenatal and postnatal influences such as social, economic, and environmental factors are taken into consideration, individual variation is more apparent than differences between unexposed and DES-exposed women.

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