Profile
Like cetrorelix (p.2084), degarelix is a gonadorelin (gonadotrophin-releasing hormone) antagonist. It is under investigation to reduce testosterone concentrations in hormonal therapy of prostate cancer.

Delmadinone Acetate *(BANM, USAN, rINNM)*

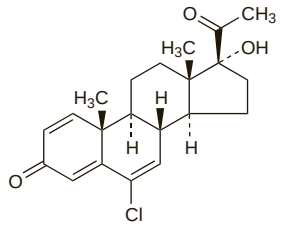
Acetato de delmadinona; Delmadinonacetat; Delmadinone, Acétate de; Delmadinoni Acetas; Delmadinoniasetaatti; RS-1301. 6-Chloro-17α-hydroxypregna-1,4,6-triene-3,20-dione acetate.

Дельмадинона Ацетат

$C_{23}H_{27}ClO_4$ = 402.9.

CAS — 15262-77-8 (delmadinone); 13698-49-2 (delmadinone acetate).

ATC Vet — QG03DX91.



(delmadinone)

Profile
Delmadinone acetate is a progestogen with anti-androgenic and anti-oestrogenic activity. It is used as an anti-androgen in veterinary practice.

Deslorelin *(BAN, USAN, rINN)* ⊗

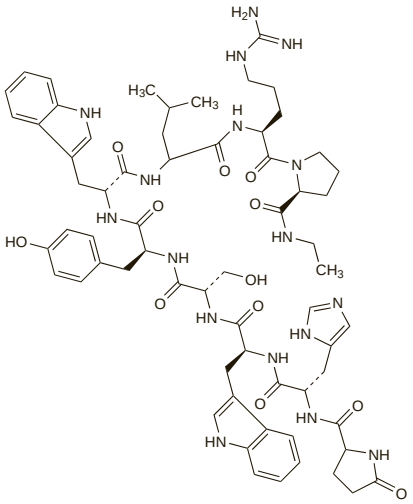
Deslorelina; Desloréline; Deslorelinum; D-Trp LHRH-PEA. 5-Oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-tryptophyl-L-leucyl-L-arginyl-*N*-ethyl-L-prolinamide.

Дезлорелин

$C_{64}H_{83}N_{17}O_{12}$ = 1282.5.

CAS — 57773-65-6.

ATC Vet — QH01CA93.



Profile
Deslorelin is an analogue of gonadorelin (p.2106) that has been investigated in the treatment of precocious puberty, short stature, prostate cancer, and endometriosis.

◊ References.

1. Anonymous. Deslorelin: D-Trp-LHRH-PEA, LHRH agonist analogue, Somagard. *Drugs R D* 1999; **2:** 420–2.
2. Klein KO, *et al.* Increased final height in precocious puberty after long-term treatment with LHRH agonists: the National Institutes of Health experience. *J Clin Endocrinol Metab* 2001; **86:** 4711–16.
3. Yanovski JA, *et al.* Treatment with a luteinizing hormone-releasing hormone agonist in adolescents with short stature. *N Engl J Med* 2003; **348:** 908–17.

Desogestrel *(BAN, USAN, rINN)*

Desogestreeli; Désogestrel; Desogestrelum; Dezogestrel; Org-2969. 13β-Ethyl-11-methylene-18,19-dinor-17α-pregn-4-en-20-yn-17β-ol.

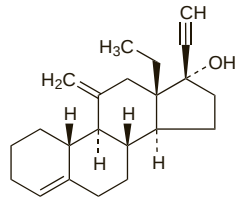
Дезогестрел

$C_{22}H_{30}O$ = 310.5.

CAS — 54024-22-5.

ATC — G03AC09.

ATC Vet — QG03AC09.



Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Desogestrel). A white or almost white, crystalline powder. Practically insoluble in water; freely soluble in dehydrated alcohol and in dichloromethane; very soluble in methyl alcohol.

Adverse Effects and Precautions

As for progestogens in general (see Progesterone, p.2125). See also under Hormonal Contraceptives, p.2059. When used as a progestogen-only contraceptive, irregular bleeding is more common with desogestrel than with other progestogen-only preparations. Desogestrel is reported to have few androgenic effects, and to have less adverse effect on the serum lipid profile than older 19-nortestosterone derivatives. However, there is some evidence that desogestrel-containing combined oral contraceptives are associated with a small increased risk of venous thromboembolism (see p.2063, and for precautions, see p.2066).

Interactions

As for progestogens in general (see Progesterone, p.2126). See also under Hormonal Contraceptives, p.2067.

Pharmacokinetics

After oral doses, desogestrel undergoes oxidative transformation in the intestinal mucosa and liver to its active metabolite 3-keto-desogestrel (etonogestrel—see p.2103).

◊ References.

1. Madden S, *et al.* Metabolism of the contraceptive steroid desogestrel by the intestinal mucosa. *Br J Clin Pharmacol* 1989; **27:** 295–9.
2. Madden S, *et al.* Metabolism of the contraceptive steroid desogestrel by human liver in vitro. *J Steroid Biochem* 1990; **35:** 281–8.
3. Kuhnz W, *et al.* Protein binding of the contraceptive steroids gestodene, 3-keto-desogestrel and ethinyloestradiol in human serum. *J Steroid Biochem* 1990; **35:** 313–18.
4. Kuhnz W, *et al.* Pharmacokinetics and serum protein binding of 3-keto-desogestrel in women during three cycles of treatment with a low-dose combination oral contraceptive. *Arzneimittelforschung* 1992; **42:** 1142–6.
5. Timmer CJ, *et al.* Bioavailability and bioequivalence of etonogestrel from two oral formulations of desogestrel: Cerazette and Liseta. *Eur J Drug Metab Pharmacokinet* 1999; **24:** 335–43.
6. Verhoeven CH, *et al.* Excretion and metabolism of desogestrel in healthy postmenopausal women. *J Steroid Biochem Mol Biol* 2001; **78:** 471–80.
7. Korhonen T, *et al.* The role of CYP2C and CYP3A in the disposition of 3-keto-desogestrel after administration of desogestrel. *Br J Clin Pharmacol* 2005; **60:** 69–75.

Uses and Administration

Desogestrel is a progestogen (see Progesterone, p.2126) structurally related to levonorgestrel that is used as a hormonal contraceptive (see p.2069). A typical daily dose of 150 micrograms is used as the progestogenic component of monophasic combined oral contraceptive preparations. Doses of 50 to 150 micrograms daily may be used in triphasic combined preparations. A dose of 75 micrograms daily is used as an oral progestogen-only contraceptive; unlike traditional progestogen-only contraceptives, desogestrel is said to reliably inhibit ovulation. Progestogen-only contraceptive efficacy is reduced if a dose of desogestrel is delayed by more than 12 hours.

Contraception. The effects of a progestogen-only contraceptive containing desogestrel have been reported.[1-3] Oral desogestrel has also been investigated as a male contraceptive, combined with testosterone given by intramuscular injection,[4] subcutaneous implant,[5,6] or transdermal patch.[7]

1. Collaborative study group on the desogestrel-containing progestogen-only pill. A double-blind study comparing the contraceptive efficacy, acceptability and safety of two progestogen-only pills containing desogestrel 75 micrograms/day or levonorgestrel 30 micrograms/day. *Eur J Contracept Reprod Health Care* 1998; **3:** 169–78.
2. Rice CF, *et al.* A comparison of the inhibition of ovulation achieved by desogestrel 75 μg and levonorgestrel 30 μg daily. *Hum Reprod* 1999; **14:** 982–5.
3. Korver T, *et al.* Maintenance of ovulation inhibition with the 75-μg desogestrel-only contraceptive pill (Cerazette) after scheduled 12-h delays in tablet intake. *Contraception* 2005; **71:** 8–13.
4. Wu FCW, *et al.* Oral progestogen combined with testosterone as a potential male contraceptive: additive effects between desogestrel and testosterone enanthate in suppression of spermatogenesis, pituitary-testicular axis, and lipid metabolism. *J Clin Endocrinol Metab* 1999; **84:** 112–22.
5. Kinniburgh D, *et al.* Oral desogestrel with testosterone pellets induces consistent suppression of spermatogenesis to azoospermia in both Caucasian and Chinese men. *Hum Reprod* 2002; **17:** 1490–1501.
6. Anderson RA, *et al.* Investigation of hormonal male contraception in African men: suppression of spermatogenesis by oral desogestrel with depot testosterone. *Hum Reprod* 2002; **17:** 2869–77.
7. Hair WM, *et al.* A novel male contraceptive pill-patch combination: oral desogestrel and transdermal testosterone in the suppression of spermatogenesis in normal men. *J Clin Endocrinol Metab* 2001; **86:** 5201–9.

Preparations

USP 31: Desogestrel and Ethinyl Estradiol Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Cerazette; ***Austria:*** Cerazette; ***Belg.:*** Cerazette; ***Braz.:*** Cerazette; Kelly; ***Chile:*** Arlette; Cerazette; Nogesta; Vanish; ***Cz.:*** Azalia; Cerazette; ***Denm.:*** Cerazette; ***Fin.:*** Cerazette; ***Fr.:*** Cerazette; ***Ger.:*** Cerazette; ***Gr.:*** Cerazette; ***Hung.:*** Cerazette; ***Indon.:*** Cerazette; ***Israel:*** Cerazette; ***Ital.:*** Cerazette; ***Mex.:*** Cerazette; ***Neth.:*** Cerazette; ***Norw.:*** Cerazette; ***NZ:*** Cerazette; ***Philipp.:*** Cerazette; ***Pol.:*** Cerazette; ***Port.:*** Cerazette; ***Rus.:*** Cerazette (Чарозетта); ***Spain:*** Cerazet; ***Swed.:*** Cerazette; ***Switz.:*** Cerazette; ***UK:*** Cerazette; ***Venez.:*** Arlette; Cerazette.

Multi-ingredient: ***Arg.:*** Marvelon; Mercilon; ***Austral.:*** Marvelon; ***Austria:*** Gracial; Laurina; Liberel; Liseta†; Marvelon; Mercilon; ***Belg.:*** Desorelle; Gracial; Marvelon; Mercilon; Ovidol; ***Braz.:*** Femina; Gestradiol; Gracial; Malu; Mercilon; Mercilon Conti; Microdiol; Minian; Novial; Primera; ***Canad.:*** Marvelon; Ortho-Cept; ***Chile:*** Ciclidon; Dal; Desoren; Gracial; Gynostat; Marvelon; Midalet; Miniestrel; Neolette; ***Cz.:*** Gracial; Jenetten†; Laurina; Marvelon; Mercilon; Novynette; Regulon; Vilonet†; ***Denm.:*** Desorelle; Gracial; Marvelon; Mercilon; Novynette; ***Fin.:*** Gracial; Marvelon; Mercilon; ***Fr.:*** Cycleane; Mercilon; Varnoline; ***Ger.:*** Biviol; Cyclosa; Desmin; Lamuna; Lovelle; Marvelon; Novial; Oviol; ***Gr.:*** Gracial; Laurina; Marvelon; Mercilon; ***Hong Kong:*** Gracial; Marvelon; Mercilon; Novynette; ***Hung.:*** Gracial; Marvelon; Mercilon; Novynette; Regulon; ***India:*** Femilon; Novelon; ***Indon.:*** Marvelon; Mercilon; ***Irl.:*** Marviol; Mercilon; ***Israel:*** Feminet; Mercilon; Microdiol; ***Ital.:*** Dueva; Gracial; Mercilon; Planum; Practil; Securgin; ***Malaysia:*** Marvelon; Mercilon; Novynette; Regulon; ***Mex.:*** Marvelon; Mercilon; Novial; ***Neth.:*** Gracial; Marvelon; Mercilon; Ovidol; ***Norw.:*** Marvelon; ***NZ:*** Marvelon; Mercilon; Trimiron†; ***Philipp.:*** Gracial; Marvelon; Mercilon; ***Pol.:*** Marvelon; Mercilon; Novynette; Regulon; ***Port.:*** Gracial; Laurina; Marvelon; Mercilon; Novynette; Regulon; ***Rus.:*** Marvelon (Марвелон); Mercilon (Мерсилон); Novynette (Новинет); Regulon (Регулон); Tri-Merci (Три-Мерси); ***S.Afr.:*** Marvelon; Mercilon; ***Singapore:*** Marvelon; Mercilon; ***Spain:*** Gracial; Microdiol; Suavuret; ***Swed.:*** Desolett; Mercilon; Trimiron; ***Switz.:*** Gracial; Marvelon; Mercilon; ***Thai.:*** Marvelon; Mercilon; Oilezz; ***Turk.:*** Desolett; Myralon; ***UK:*** Marvelon; Mercilon; ***USA:*** Apri; Cesia; Cyclessa; Desogen; Kariva; Mircette; Ortho-Cept; Reclipsen; Solia; Velivet; ***Venez.:*** Ciclidon; Marvelon; Mercilon; Mipil; Novial.

Dienestrol *(BAN, rINN)*

Dehydrostilbestrol; Dièn estrol; Dienestroli; Dienestrolis; Dienestrolum; Dienoestrol; Dienoestrolum; Dienösztrol; Oestrodienolum. *(E,E)*-4,4′-[Di(ethylidene)ethylene]diphenol; 4,4′-(1,2-Diethylidene-1,2-ethanediyl)bisphenol.

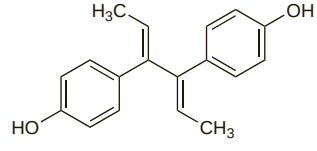
Диенэстрол

$C_{18}H_{18}O_2$ = 266.3.

CAS — 84-17-3 (dienestrol); 13029-44-2 ((E,E)-dienestrol).

ATC — G03CB01.

ATC Vet — QG03CB01; QG03CC02.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Dienestrol). A white or almost white, crystalline powder. Practically insoluble in water; freely soluble in alcohol and in acetone; dissolves in dilute solutions of alkali hydroxides. Protect from light.

USP 31 (Dienestrol). Colourless, white, or practically white needle-like crystals, or white or practically white crystalline

powder. It is odourless. Practically insoluble in water; soluble in alcohol, in acetone, in ether, in methyl alcohol, in propylene glycol, and in solutions of alkali hydroxides; slightly soluble in chloroform and in fatty oils.

Profile

Dienestrol is a synthetic nonsteroidal oestrogen structurally related to diethylstilbestrol (p.2094). It has been used as a 0.01% cream in the treatment of menopausal atrophic vaginitis. If used on a long-term basis in women with a uterus a progestogen is required.

Dienestrol diacetate has been used as an ingredient of topical preparations for skin disorders.

Porphyria. Dienestrol is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals* or *in-vitro* systems.

Preparations

USP 31: Dienestrol Cream.

Proprietary Preparations (details are given in Part 3)
Denm.: Sexadien†; ***USA:*** Ortho-Dienestrol.

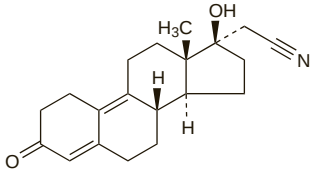
Dienogest *(BAN, USAN, rINN)*

Diénogest; Dienogesti; Dienogestum; STS-557. 17-Hydroxy-3-oxo-19-nor-17α-pregna-4,9-diene-21-nitrile.

Диеногест

$C_{20}H_{25}NO_2$ = 311.4.

CAS — 65928-58-7.



Profile

Dienogest is a nonethinylated progestogen (see Progesterone, p.2125) structurally related to nortestosterone. It is reported to have anti-androgenic properties. Dienogest is used as the progestogen component of some combined oral contraceptives (see p.2058); a typical daily dose is 2 mg. It is also used as the progestogen component in menopausal HRT (see p.2071) in a daily dose of 2 mg.

◊ Reviews.

1. Foster RH, Wilde MI. Dienogest. *Drugs* 1998; **56:** 825–33.
2. Wellington K, Perry CM. Estradiol valerate/dienogest. *Drugs* 2002; **62:** 491–504.

Preparations

Proprietary Preparations (details are given in Part 3)
Port.: Jeanine.

Multi-ingredient: ***Austral.:*** Valette; ***Austria:*** Climodien; Jeanine; Lafamme; Valette; ***Belg.:*** Climodien; ***Cz.:*** Jeanine; Klimodien; ***Denm.:*** Climodien; ***Fr.:*** Climodiene; ***Ger.:*** Climodien; Lafamme; Valette; ***Gr.:*** Climodien†; ***Hung.:*** Klimodien†; ***Neth.:*** Climodien; Lafamme; ***Norw.:*** Climodien; ***Pol.:*** Jeanine; ***Port.:*** Climodien; Lafamme; Valette; ***Rus.:*** Climodien (Климодиен); Jeanine (Жанин); ***Spain:*** Climodien; Mevaren; ***Swed.:*** Climodien; ***Turk.:*** Climodien.

Diethylstilbestrol *(BAN, rINN)*

DES; Diéthylstilbestrol; Dietylstilbestrolum; Diethylstilboestrol; Dietilestilbestrol; Dietilstilbestrolis; Dietilstilbösztrol; Dietylstilbestrol; Dietyylistilbestroli; NSC-3070; Stilbestrol; Stilboestrol. (*E*)-αβ-Diethylstilbene-4-4′-diol.

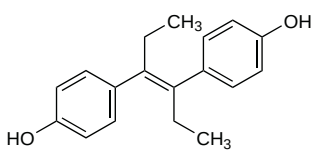
Диэтилстильбэстрол

$C_{18}H_{20}O_2$ = 268.4.

CAS — 56-53-1.

ATC — G03CB02; L02AA01.

ATC Vet — QG03CB02; QG03CC05; QL02AA01.



Pharmacopoeias. In *Chin., Eur.* (see p.vii), and *US.*
Ph. Eur. 6.2 (Diethylstilbestrol). A white or almost white crystalline powder. Practically insoluble in water; freely soluble in alcohol; dissolves in solutions of alkali hydroxides. Protect from light.

USP 31 (Diethylstilbestrol). A white, odourless, crystalline powder. Practically insoluble in water; soluble in alcohol, in chloroform, in ether, in fatty oils, and in dilute alkali hydroxides. Store in airtight containers. Protect from light.

Diethylstilbestrol Dipropionate *(BANM, rINNM)*

Diéthylstilbestrol, Dipropionate de; Diethylstilbestroli Dipropionas; Dipropionato de dietilestilbestrol; Stilboestrol Dipropionate. (*E*)-αβ-Diethylstilbene-4,4′-diol dipropionate.

Диэтилстильбэстрола Дипропионат

$C_{24}H_{28}O_4$ = 380.5.

CAS — 130-80-3.

ATC — G03CB02; L02AA01.

ATC Vet — QG03CB02; QL02AA01.

Adverse Effects and Precautions

Dose-related adverse effects of diethylstilbestrol include nausea, fluid retention, and arterial and venous thrombosis, and these effects are common at the doses used for palliation of cancer. Impotence and gynaecomastia occur in men, and withdrawal bleeding may occur in women, as may hypercalcaemia and bone pain in women treated for breast cancer. Diethylstilbestrol should be used with caution in those with cardiovascular disease or renal or hepatic impairment. Use of diethylstilbestrol is contra-indicated if pregnancy is suspected.

Adverse effects and precautions of oestrogens in general (steroidal compounds) are covered under Estradiol, on p.2097.

Historically, high doses of diethylstilbestrol and related substances were used for 'hormonal support' in pregnant women to try to prevent miscarriages and preterm births, most commonly in the USA. This practice was later shown to be ineffective. Adverse effects on the genito-urinary tract of offspring of these women have been noted. In particular, an increased incidence of changes in the cervix and vagina including adenosis and rarely clear-cell adenocarcinoma has been seen in postpubertal daughters of women who received diethylstilbestrol or related substances during pregnancy (see below). A possible increased incidence of abnormalities of the genital tract and of abnormal spermatozoa has been reported in male offspring similarly exposed (see below). The recipients themselves appear to be at a small increased risk of breast cancer (see below).

Carcinogenicity. ***BREAST.*** No statistically significant difference in the incidence of breast cancer was found among a group of 693 women given diethylstilbestrol during pregnancy 25 years earlier compared with a control group of 668 who were not.[1] This finding was, however, criticised[2] on the basis that the study lacked the statistical power to reject the null hypothesis. In another study[3] the incidence of breast cancer in 3033 women who had taken diethylstilbestrol in pregnancy during the period 1940 to 1960 was compared with the incidence in a comparable group of unexposed women. This study involved over 85 000 women-years of follow-up in each group and it was found that the incidence of breast cancer per 100 000 women-years was 134 in the exposed group and 93 in the unexposed group (a relative risk of 1.4). The authors concluded that in those women given diethylstilbestrol there was a moderately increased incidence of breast cancer but that some unrecognised concomitant of exposure could not be excluded as a possibility for the increase. Although this study suggested that the risk increased over time, subsequent follow-up,[4] while confirming a modest increase in risk overall, did not confirm a higher risk in these women as time went on. Further follow-up and analysis[5] of the combined data from these cohort studies[1,3,4] confirmed a modest increase in risk of breast cancer associated with diethylstilbestrol (relative risk 1.27, 95% confidence interval 1.07 to 1.52). Another large population cohort study[6] suggested that the risk of fatal breast cancer might also be increased in women who had been given diethylstilbestrol.

Two cases of breast cancer[7] in premenopausal women exposed to diethylstilbestrol *in utero* have raised the possibility that the risk of breast cancer may be increased in these women, in addition to the known genito-urinary risk (see below under Pregnancy, Effects on Female Offspring). However, a cohort study[8] involving 4536 women exposed *in utero* found no increased risk of other cancers overall, and did not show an increased risk of breast cancer (relative risk 1.18; 95% confidence intervals 0.56 to 2.49). A later study[9] of further follow-up of this cohort, plus additional data from another group, found that although the risk overall and for younger women was not increased, from the age of 40 years the risk increased to 1.91 (95% confidence interval 1.09 to 3.33). The risk appeared to increase further with greater age, but the relatively small number of cases in women aged 50 years and over made this harder to establish.

1. Bibbo M, *et al.* A twenty-five-year follow-up study of women exposed to diethylstilbestrol during pregnancy. *N Engl J Med* 1978; **298:** 763–7.
2. Clark LC, Portier KM. Diethylstilbestrol and the risk of cancer. *N Engl J Med* 1979; **300:** 263–4.
3. Greenberg ER, *et al.* Breast cancer in mothers given diethylstilbestrol in pregnancy. *N Engl J Med* 1984; **311:** 1393–8.
4. Colton T, *et al.* Breast cancer in mothers prescribed diethylstilbestrol in pregnancy. *JAMA* 1993; **269:** 2096–2100.
5. Titus-Ernstoff L, *et al.* Long-term cancer risk in women given diethylstilbestrol (DES) during pregnancy. *Br J Cancer* 2001; **84:** 126–33.
6. Calle EE, *et al.* Diethylstilbestrol and risk of fatal breast cancer in a prospective cohort of US women. *Am J Epidemiol* 1996; **144:** 645–52.
7. Huckell C, *et al.* Premenopausal breast cancer after in-utero exposure to stilboestrol. *Lancet* 1996; **348:** 331.
8. Hatch EE, *et al.* Cancer risk in women exposed to diethylstilbestrol in utero. *JAMA* 1998; **280:** 630–4.
9. Palmer JR, *et al.* Prenatal diethylstilbestrol exposure and risk of breast cancer. *Cancer Epidemiol Biomarkers Prev* 2006; **15:** 1509–14.

GENITO-URINARY TRACT. See below under Pregnancy, Effects on Female Offspring.

KIDNEY. Renal carcinoma was associated with the long-term use of diethylstilbestrol for prostate cancer in 2 men.[1]

1. Nissenkorn I, *et al.* Oestrogen-induced renal carcinoma. *Br J Urol* 1979; **51:** 6–9.

LIVER. Hepatic angiosarcoma developed in a 76-year-old man who had received diethylstilbestrol 3 mg daily for 12 years.[1] Hepatoma developed in another elderly man who had received a similar dose for 4.5 years.[2]

1. Hoch-Ligeti C. Angiosarcoma of the liver associated with diethylstilbestrol. *JAMA* 1978; **240:** 1510–11.
2. Brooks JJ. Hepatoma associated with diethylstilbestrol therapy for prostate carcinoma. *J Urol (Baltimore)* 1982; **128:** 1044–5.

Effects on the blood. Adverse haematological effects reported with diethylstilbestrol have included severe bone-marrow changes in a 71-year-old man given diethylstilbestrol in a massive dose of 150 mg daily for 7 years[1] and fatal immune haemolytic anaemia in a 69-year-old man given weekly infusions of diethylstilbestrol 1 g for 9 weeks.[2] The latter reaction was due to an IgG antibody specific for diethylstilbestrol.

1. Anderson AL, Lynch EC. Myelodyspoietic syndrome associated with diethylstilbestrol therapy. *Arch Intern Med* 1980; **140:** 976–7.
2. Rosenfeld CS, *et al.* Diethylstilbestrol-associated hemolytic anemia with a positive direct antiglobulin test result. *Am J Med* 1989; **86:** 617–18.

Pregnancy. ***EFFECTS ON FEMALE OFFSPRING.*** The DESAD (Diethylstilbestrol and Adenosis) Project carried out by the National Cancer Institute in the USA led to several reports linking exposure to diethylstilbestrol *in utero* to adverse genital-tract effects.[1-3] It was reported that of nearly 300 young females with clear-cell adenocarcinoma of the genital tract, more than 80% had been exposed *in utero* to diethylstilbestrol-type hormones.[1] Patients had been aged 7 to 28 years at the time of diagnosis. Doses and duration of treatment varied widely; the association existed for both 1.5 mg of diethylstilbestrol daily throughout pregnancy and variable amounts for a week or more during the first trimester. Vaginal adenosis, rare in unexposed young women, was present in about a third of those exposed in the first 4 months of pregnancy, and cervical ectropion in more than two-thirds. Vaginal epithelial changes were most closely associated with early exposure to diethylstilbestrol, with the total dose, and with the duration of exposure; their incidence decreased with age. The risk of cancer in the first 25 years after exposure was small.[2] Fertility did not appear to be impaired in women who had been exposed *in utero* to diethylstilbestrol but the relative risk of an unfavourable outcome of pregnancy in such a group was 1.69. However, of the women who became pregnant, 81% of those exposed to diethylstilbestrol and 95% of control subjects had at least one full-term live birth.[3] In a review of vaginal adenosis and its association with maternal diethylstilbestrol ingestion during pregnancy[4] it was noted that the link between diethylstilbestrol and particularly the benign changes in the vagina and cervix (adenosis) seemed well established. The association between this drug and the development of genital malignancies was less clear, and the very low incidence in the prospective studies in the USA supported this concept. The problem was rare in the UK, but clinicians should be aware that it existed. Cases of vaginal adenosis in young women should be investigated and screened appropriately, and preferably referred to centres where colposcopic expertise was available. Treatment of simple vaginal adenosis should be avoided.

Later reviews[5,6] have highlighted the fact that adverse effects were still emerging in women who had been exposed to diethylstilbestrol *in utero* several decades before. The need for thorough medical screening of such women was emphasised; genital-tract examination was particularly important. It was pointed out[6] that many women exposed to diethylstilbestrol *in utero* were in the