

ORTHO TRI-CYCLE[®] TABLETS
ORTHO-CYCLE[®] TABLETS
(norgestimate/ethinyl estradiol)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.



DESCRIPTION
Each of the following products is a combination oral contraceptive containing the progestational compound norgestimate and the estrogenic compound ethinyl estradiol. ORTHO TRI-CYCLE[®] Tablets.

Each white tablet contains 0.180 mg of the progestational compound, norgestimate (18,19-Di-nor-17-pregn-4-en-20-yn-3-one, 17-(acetoxyloxy)-13-ethyl-,oxime,(17 α)-(+)- and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17 α -pregna-1,3,5(10)-trien-20-yn-3,17-diol). Inactive ingredients include carnauba wax, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, purified water and titanium dioxide.

Each light blue tablet contains 0.215 mg of the progestational compound norgestimate (18,19-Di-nor-17-pregn-4-en-20-yn-3-one, 17-(acetoxyloxy)-13-ethyl-,oxime,(17 α)-(+)- and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17 α -pregna-1,3,5(10)-trien-20-yn-3,17-diol). Inactive ingredients include FD & C Blue No. 2 Aluminum Lake, carnauba wax, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, purified water and titanium dioxide.

Each blue tablet contains 0.250 mg of the progestational compound norgestimate (18,19-Di-nor-17-pregn-4-en-20-yn-3-one, 17-(acetoxyloxy)-13-ethyl-,oxime,(17 α)-(+)- and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17 α -pregna-1,3,5(10)-trien-20-yn-3,17-diol). Inactive ingredients include FD & C Blue No. 2 Aluminum Lake, carnauba wax, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, purified water and titanium dioxide.

Each dark green tablet contains only inert ingredients, as follows: FD & C Blue No. 2 Aluminum Lake, ferric oxide, hypromellose, lactose, magnesium stearate, polyethylene glycol, pregelatinized corn starch, purified water, talc and titanium dioxide.

ORTHO-CYCLE[®] Tablets.
Each blue tablet contains 0.250 mg of the progestational compound norgestimate (18,19-Di-nor-17-pregn-4-en-20-yn-3-one, 17-(acetoxyloxy)-13-ethyl-,oxime,(17 α)-(+)- and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17 α -pregna-1,3,5(10)-trien-20-yn-3,17-diol). Inactive ingredients include FD & C Blue No. 2 Aluminum Lake, carnauba wax, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, purified water and titanium dioxide.

Each dark green tablet contains only inert ingredients, as follows: FD & C Blue No. 2 Aluminum Lake, ferric oxide, hypromellose, lactose, magnesium stearate, polyethylene glycol, pregelatinized corn starch, purified water, talc and titanium dioxide.

Chemical Structures:

CLINICAL PHARMACOLOGY
Oral Contraception
Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which reduce the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

Receptor binding studies, as well as studies in animals and humans, have shown that norgestimate and 17-deacetyl norgestimate, the major serum metabolite, combine high progesterational activity with minimal androgenic activity. Norgestimate, in combination with ethinyl estradiol, does not counteract the estrogen-induced increases in sex hormone binding globulin (SHBG), resulting in lower serum testosterone.^{20,21,24}

Acne
Acne is a skin condition with a multifactorial etiology, including androgen stimulation of sebaceous production. While the combination of ethinyl estradiol and norgestimate increases sex hormone binding globulin (SHBG) and decreases free testosterone, the relationship between these changes and a decrease in the severity of facial acne in otherwise healthy women with this skin condition has not been established.

PHARMACOKINETICS
Absorption
Norgestimate (NGM) and ethinyl estradiol (EE) are rapidly absorbed following oral administration. Norgestimate is rapidly and completely metabolized by firstpass (intestinal and/or hepatic) mechanisms to norgestrelom (NGNM) and norgestrel (NG), which are the major active metabolites of norgestimate.

Peak serum concentrations of NGM and EE are generally reached by 2 hours after administration of ORTHO-CYCLE[®] or ORTHO TRI-CYCLE[®]. Accumulation following multiple dosing of the 250 µg NGM / 35 µg dose is approximately 2-fold for NGM and EE compared with single dose administration. The pharmacokinetics of NGM is dose proportional following NGM doses of 180 µg to 250 µg. Steady-state concentration of EE is achieved by Day 7 of each dosing cycle. Steady-state concentration of NGM and NG are achieved by Day 21. Non-linear accumulation (approximately 8 fold) of norgestrel is observed as a result of high affinity binding to SHBG (sex hormone-binding globulin), which limits its biological activity.

Table I. Summary of norgestrelom, norgestrel and ethinyl estradiol pharmacokinetic parameters.

Table II. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table III. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table IV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table V. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table VI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table VII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table VIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table IX. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table X. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XI. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XIII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XIV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XV. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XVI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XVII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XVIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XIX. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XX. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXI. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXIII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXIV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXV. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXVI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXVII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXVIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXIX. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXX. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXI. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXIII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXIV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXV. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXVI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXVII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXVIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXIX. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXX. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXXI. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXXIII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXIV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXXV. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXVI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXXVII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXVIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

ORTHO TRI-CYCLE[®] TABLETS
ORTHO-CYCLE[®] TABLETS
(norgestimate/ethinyl estradiol)

Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.



DESCRIPTION
Each of the following products is a combination oral contraceptive containing the progestational compound norgestimate and the estrogenic compound ethinyl estradiol. ORTHO TRI-CYCLE[®] Tablets.

Each white tablet contains 0.180 mg of the progestational compound, norgestimate (18,19-Di-nor-17-pregn-4-en-20-yn-3-one, 17-(acetoxyloxy)-13-ethyl-,oxime,(17 α)-(+)- and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17 α -pregna-1,3,5(10)-trien-20-yn-3,17-diol). Inactive ingredients include carnauba wax, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, purified water and titanium dioxide.

Each light blue tablet contains 0.215 mg of the progestational compound norgestimate (18,19-Di-nor-17-pregn-4-en-20-yn-3-one, 17-(acetoxyloxy)-13-ethyl-,oxime,(17 α)-(+)- and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17 α -pregna-1,3,5(10)-trien-20-yn-3,17-diol). Inactive ingredients include FD & C Blue No. 2 Aluminum Lake, carnauba wax, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, purified water and titanium dioxide.

Each blue tablet contains 0.250 mg of the progestational compound norgestimate (18,19-Di-nor-17-pregn-4-en-20-yn-3-one, 17-(acetoxyloxy)-13-ethyl-,oxime,(17 α)-(+)- and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17 α -pregna-1,3,5(10)-trien-20-yn-3,17-diol). Inactive ingredients include FD & C Blue No. 2 Aluminum Lake, carnauba wax, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, purified water and titanium dioxide.

Each dark green tablet contains only inert ingredients, as follows: FD & C Blue No. 2 Aluminum Lake, ferric oxide, hypromellose, lactose, magnesium stearate, polyethylene glycol, pregelatinized corn starch, purified water, talc and titanium dioxide.

ORTHO-CYCLE[®] Tablets.
Each blue tablet contains 0.250 mg of the progestational compound norgestimate (18,19-Di-nor-17-pregn-4-en-20-yn-3-one, 17-(acetoxyloxy)-13-ethyl-,oxime,(17 α)-(+)- and 0.035 mg of the estrogenic compound, ethinyl estradiol (19-nor-17 α -pregna-1,3,5(10)-trien-20-yn-3,17-diol). Inactive ingredients include FD & C Blue No. 2 Aluminum Lake, carnauba wax, croscarmellose sodium, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbate 80, purified water and titanium dioxide.

Each dark green tablet contains only inert ingredients, as follows: FD & C Blue No. 2 Aluminum Lake, ferric oxide, hypromellose, lactose, magnesium stearate, polyethylene glycol, pregelatinized corn starch, purified water, talc and titanium dioxide.

Chemical Structures:

CLINICAL PHARMACOLOGY
Oral Contraception
Combination oral contraceptives act by suppression of gonadotropins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which reduce the difficulty of sperm entry into the uterus) and the endometrium (which reduce the likelihood of implantation).

Receptor binding studies, as well as studies in animals and humans, have shown that norgestimate and 17-deacetyl norgestimate, the major serum metabolite, combine high progesterational activity with minimal androgenic activity. Norgestimate, in combination with ethinyl estradiol, does not counteract the estrogen-induced increases in sex hormone binding globulin (SHBG), resulting in lower serum testosterone.^{20,21,24}

Acne
Acne is a skin condition with a multifactorial etiology, including androgen stimulation of sebaceous production. While the combination of ethinyl estradiol and norgestimate increases sex hormone binding globulin (SHBG) and decreases free testosterone, the relationship between these changes and a decrease in the severity of facial acne in otherwise healthy women with this skin condition has not been established.

PHARMACOKINETICS
Absorption
Norgestimate (NGM) and ethinyl estradiol (EE) are rapidly absorbed following oral administration. Norgestimate is rapidly and completely metabolized by firstpass (intestinal and/or hepatic) mechanisms to norgestrelom (NGNM) and norgestrel (NG), which are the major active metabolites of norgestimate.

Peak serum concentrations of NGM and EE are generally reached by 2 hours after administration of ORTHO-CYCLE[®] or ORTHO TRI-CYCLE[®]. Accumulation following multiple dosing of the 250 µg NGM / 35 µg dose is approximately 2-fold for NGM and EE compared with single dose administration. The pharmacokinetics of NGM is dose proportional following NGM doses of 180 µg to 250 µg. Steady-state concentration of EE is achieved by Day 7 of each dosing cycle. Steady-state concentration of NGM and NG are achieved by Day 21. Non-linear accumulation (approximately 8 fold) of norgestrel is observed as a result of high affinity binding to SHBG (sex hormone-binding globulin), which limits its biological activity.

Table I. Summary of norgestrelom, norgestrel and ethinyl estradiol pharmacokinetic parameters.

Table II. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table III. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table IV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table V. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table VI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table VII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table VIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table IX. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table X. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XI. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XIII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XIV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XV. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XVI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XVII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XVIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XIX. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XX. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXI. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXIII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXIV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXV. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXVI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXVII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXVIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXIX. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXX. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXI. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXIII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXIV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXV. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXVI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXVII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXVIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXXIX. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXX. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXXXI. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXXII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXXXIII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXXIV. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXXXV. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXXVI. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

Table XXXXXVII. Mean (SD) Pharmacokinetic Parameters of ORTHO-CYCLE[®] During a Three Cycle Study

Table XXXXXVIII. Mean (SD) Pharmacokinetic Parameters of ORTHO TRI-CYCLE[®] During a Three Cycle Study

ORTHO TRI-CYCLE[®] TABLETS
ORTHO-CYCLE[®] TABLETS
(norgestimate/ethinyl estradiol)

gathered in the 1970's.²⁵ Current clinical recommendation involves the use of lower estrogen dose formulations and a careful consideration of risk factors. In 1989, the Fertility and Maternal Health Drugs Advisory Committee was asked to review the use of oral contraceptives in women 40 years of age and over. The Committee concluded that although cardiovascular disease risks may be increased with oral contraceptive use after age 40 in healthy non-smoking women (even with the newer low-dose formulations), there are also greater potential health risks associated with pregnancy in older women and with the alternative surgical and medical procedures which may be necessary if such women do not have access to effective and acceptable means of contraception. The Committee recommended that the benefits of low-dose oral contraceptive use by healthy non-smoking women over 40 may outweigh the possible risks.

Of course, older women, as all women, who take oral contraceptives, should take an oral contraceptive which contains the least amount of estrogen and progestogen that is compatible with a low failure rate and individual patient needs.

Table IV. Annual Number of Birth-Related and Method-Related Deaths Associated With Control of Fertility Per 100,000 Non-Sterile Women, by Fertility Control Method According to Age

Method of control and outcome	15-19	20-24	25-29	30-34	35-39	40-44
No fertility control methods*	7.0	7.4	9.1	14.8	25.7	28.2
Oral contraceptives	0.3	0.5	0.9	1.9	3.8	31.6
Oral contraceptives non-smoker**						
Oral contraceptives smoker**	2.2	3.4	6.6	13.5	51.1	117.2
IUD**	0.8	0.8	1			

ORTHO TRI-CYCLEN® TABLETS
ORTHO-CYCLEN® TABLETS
(norgestimate/ethinyl estradiol)

Royal College of General Practitioners: Incidence of arterial disease among oral contraceptive users. *J Royal Coll Gen Pract* 1983; 33:75-82. 35. Ory HW. Mortality associated with fertility and fertility control. 1983. Family Planning Perspectives 1983; 15:50-56. 36. The Cancer and Steroid Hormone Study of the Centers for Disease Control and the National Institute of Child Health and Human Development. Oral contraceptives and the risk of breast cancer. *N Engl J Med* 1986; 315:405-411. 37. Pike MC, Henderson BE, Kralo MD, Duke A, Roy S. Breast cancer in young women and use of oral contraceptives: possible path of etiology of formulation and age at use. *Lancet* 1983; 2:926-929. 38. Paul C, Skyeing DG, Spears GFS, Kaldor JM, Jansen RW, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S, Breast cancer and oral contraceptives and breast cancer. A national study. *Br Med J* 1986; 293:725-729. 39. Paul C, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Oral contraceptives and the risk of early oral contraceptive use. *Obstet Gynecol* 1986; 68:863-868. 40. Olsson H, Olsson M, Moller TR, Ranslam J, Holm P. Oral contraceptive use and breast cancer in young women in Sweden (letter). *Lancet* 1985; 1(8431):746-749. 41. McPherson K, Vessey M, Neil A, Doll R, Jones L, Roberts M. Early contraceptive use and breast cancer. Results of another case-control study. *Br J Cancer* 1987; 56:653-660. 42. Huggins GR, Zucker P. Oral contraceptives and the neoplasia: 1987 update. *Fertil Steril* 1987; 47:733-761. 43. McPherson K, Diffe JO. The pill and breast cancer: why the uncertainty? *Br Med J* 1986; 293:709-710. 44. Shapiro S. Oral contraceptives – time to take stock. *N Engl J Med* 1987; 316:450-451. 45. Ory H, Nabz Z, Conger SB, Hatcher RA, Tyler CW. Contraceptive choice and prevalence of cervical dysplasia and cervical carcinoma in situ. *Am J Obstet Gynecol* 1976; 124:573-577. 46. Vessey MP, Lawless M, McPherson K, Yeates D. Neoplasia of the cervix uteri and contraception: a possible adverse effect of the pill. *Lancet* 1983; 2:930. 47. Britton LA, Huggins GR, Lehman HF, Maili K, Savitz DA, Trapido E, Rosenthal J, Hoover F. Long term use of oral contraceptives and risk of invasive cervical cancer. *Am J Epidemiol* 1987; 125:433-439. 48. WHO PD. Shapiro S. Study of Neoplasia and Steroid Contraceptives: Invasive cervical cancer and combined oral contraceptives. *Br Med J* 1985; 290:961-965. 49. Rooks JB, Ory HW, Ishak KG, Strauss LT, Greenspan JR, Hill AP, Tyler CW. Epidemiology of hepatocellular adenoma: the role of oral contraceptive use. *JAMA* 1979; 242:644-648. 50. Bein NJ, Goldsmith HS. Recurrent metastatic neurofibromatosis from benign hepatic tumors. *Am J Surg* 1977; 84:433-435. 51. Klotzsch G. Epidemiology of Hepatic tumors: possible relationship to use of oral contraceptives. *Gastroenterology* 1977; 73:386-394. 52. Henderson BE, Preston-Martin S, Edmondson HA, Peters RL, Pike MC. Hepatocellular carcinoma and oral contraceptives. *Br J Cancer* 1983; 48:437-441. 53. Neuberger J, Forman D, Doll R, Williams R. Oral contraceptives and hepatocellular carcinoma. *Br Med J* 1986; 195:1357-1357. 54. Forman D, Vinton TJ, Doll R. Cancer of the liver and oral contraceptives. *Br Med J* 1986; 292:1357-1361. 55. Harlap S, Eldor J. Births following oral contraceptive failures. *Obstet Gynecol* 1980; 55:447-452. 56. Savolainen E, Saksela E, Saanen L. Teratogenic hazards of oral contraceptives analyzed in a national malformation register. *Am J Obstet Gynecol* 1981; 114:521-524. 57. Klotzsch G, Klotzsch G, Klotzsch G. Oral contraceptives and birth defects. *Am J Epidemiol* 1980; 112:73-79. 58. Ferencz C, Matanoski GM, Wilson PD, Rubin JD, Neill CA, Gutberlet R. Maternal hormone therapy and congenital heart disease. *Teratology* 1980; 21:225-239. 59. Rothman KJ, Fryler DC, Goldblatt A, Kreidberg MB. Exogenous hormones and other drug exposures of children with congenital heart disease. *Am J Epidemiol* 1979; 109:433-439. 60. Collaborative Drug Surveillance Program. Oral contraceptives and venous thromboembolic disease, surgically confirmed gallbladder disease, and breast tumors. *Lancet* 1973; 1:1399-1401. 61. Royal College of General Practitioners. Oral contraceptives and health. New York, Plenum 1974. 62. Layde PM, Vessey MP, Yeates D. Risk of gallbladder disease: a cohort study of young women attending family planning clinics. *J Epidemiol Community Health* 1982; 36:274-280. 63. Royal College of Epidemiology and Prevention of Cholelithiasis (GREPCO). Prevalence of gallstone disease in an Italian adult female population. *Am J Epidemiol* 1984; 119:796-805. 64. Storm BL, Tamagnoni RT, Morse ML, Lazar EL, West SL, Stolley PD, Jones JK. Oral contraceptives and other risk factors for gallbladder disease. *Clin Pharmacol Ther* 1986; 39:325-331. 65. Wynn V, Adams PW, Goldstein IF, Meisner J, Nithyananthan R, Oakley NW, Seegal A. Comparison of effects of different combined oral contraceptive formulations on carbohydrate and lipid metabolism. *Lancet* 1979; 1:1045-1049. 66. Wynn V. Effect of progestins and progestins on carbohydrate metabolism. In: Progestosterone and Progesterone. *Bardin CW, Milgrom E, Mauvais-Jarvis P, eds.* Raven Press 1983; pp 395-410. 67. Perlman JA, Roussel-Uclaf RG, Lior H, Lieberknecht G. Oral glucose tolerance and the potency of oral contraceptive progestagens. *J Chronic Dis* 1985; 38:857-864. 68. Royal College of General Practitioners. Oral Contraception Study: Effect on hypertension and benign breast disease of progestogen component in combined oral contraceptives. *Lancet* 1972; 1:624. 69. Fischl IR, Frank J. Oral contraceptives and blood pressure. *JAMA* 1972; 227:2499-2503. 70. Lenz G. Oral contraceptive induced hypertension – nine years later. *Am J Obstet Gynecol* 1976; 126:141-147. 71. Ramcharan S, Peritz E, Pellegrin FA, Williams WT. Incidence of hypertension in the Walnut Creek Contraceptive Drug Study cohort. In: Pharmacology of steroid contraceptive drugs. Garattini S, Berendes HW, Eds. New York, Raven Press, 1977; pp 277-289. 72. Stolley P, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Study of Neoplasia and Steroid Contraceptives: Oral contraceptive use and the risk of endometrial cancer. *JAMA* 1987; 257:796-800. 73. Ory HW. Functional ovarian cysts and oral contraceptives: negative association confirmed surgically. *JAMA* 1974; 228:68-69. 74. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptives and reduced risk of benign breast disease. *N Engl J Med* 1976; 294:10-22. 75. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R. Oral contraceptive use and breast cancer in young women. *A Joint National Contraception Study in Sweden and Norway.* *Lancet* 1986; 1:650-654. 83. Kay CR, Hannafor PC. Breast cancer and the pill – A further report from the Royal College of General Practitioners oral contraceptive study. *Br J Cancer* 1988; 58:675-680. 84. Stadel BV, La S. Schlesselman JJ, Murray P. Oral contraceptives and premalignant breast cancer in nulliparous women. *Contraception* 1988; 38:287-299. 85. Miller DR, Rosenberg L, Kaufman DW, Stolley P, Warshawer M, Shapiro S. Breast cancer before age 45 and oral contraceptive use. *New Findings.* *Am J Epidemiol* 1989; 129:269-280. 86. The UK National Case-Control Study. Oral contraceptive use and breast cancer in young women. *Lancet* 1985; 1:973-982. 87. Schlesselman JJ. Cancer of the breast and endometrial cancer in relation to use of oral contraceptives. *Contraception* 1989; 40:1-38. 88. Vessey MP, McPherson K, Villard-Mackintosh L, Yeates D. Oral contraceptives and cancer: latest findings in a large cohort study. *Br J Cancer* 1989; 59:613-617. 89. Jick SS, Walker AM, Stergachis A, Jick H. Oral contraceptives and breast cancer. *Br J Cancer* 1989; 60:104-122. 77. Ory HW, Cole P, MacMahon B, Hoover R.