Combined Oral Contraceptives for the Treatment of Acne: A Practical Guide

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Many therapies exist in the arsenal of drugs available to dermatologists for the treatment of acne vulgaris. Among them, hormonal therapy stands out as a unique and highly efficacious treatment modality. Although some dermatologists may be hesitant to prescribe hormonal therapies, they can be safely and appropriately used in eligible female patients to treat acne vulgaris. Herein, current issues regarding the hormonal treatment of acne in the form of combined oral contraceptives (COCs) are presented, and a practical method for implementing this therapy is proposed. Specifically, drug selection, associated risks, benefits, monitoring, and counseling are discussed, with emphasis on the practicality of use in the clinical setting.

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Hormonal therapy in the form of combined oral contraceptives (COCs) can be a useful tool in the treatment of patients with mild, moderate, or severe acne vulgaris.[1,2] Eligible patients include postmenarcheal to premenopausal women who desire contraception or simply do not intend to become pregnant. Combined oral contraceptives may be used in combination with other acne treatments, and they can be considered as first-line agents in patients with a strong association between acne severity and their menstrual cycle or in the presence of menstrual cycle irregularities. Although there has been concern that the contraceptive ability of COCs is decreased by concomitant use of antibiotics, failure rates were no higher than the typical COC failure rates of 1% to 3%.[3] There is no pharmacokinetic evidence to indicate that any antibiotics other than rifampin lower levels of COCs.[4]

Adrenal or ovarian neoplasms should be excluded by history and physical examination prior to initiating treatment with COCs. Hirsutism, alopecia, acanthosis nigricans, cushingoid symptoms, irregular menses, clitoromegaly, or severe acne of sudden onset warrant further endocrinologic testing.[5-7] Menstrual irregularity in the first 2 to 3 years of postmenarcheal females is common and usually does not require further workup.[8]

Drug Selection

Combined oral contraceptives are effective in the treatment of acne but vary in their formulation.[9-12] All COCs combine an estrogen, typically ethinyl estradiol (EE), and a progestin. First-generation COCs consisted of 50 to 150 μg of estrogens as well as progestins called estranes (eg, norethindrone, ethynodiol diacetate). Second-generation COCs dosed estrogen at less than 50 μg combined with gonane progestins (eg, levonorgestrel, norgestimate). Third-generation COCs also used less androgenic gonane progestins (eg, desogestrel, gestodene). A fourth generation has been proposed that consists of COCs using progestins, such as drospirenone (DRSP) and chlormadinone acetate, which are not testosterone derived.[13] Theoretically, less androgenic COCs should be better acne treatments.[5,14-16] However, all COCs effectively treat acne, and there is little evidence to suggest one is substantially more effective than the next.[17-19] Therefore, it is believed that the estrogen component may be more responsible for the therapeutic effects of COCs via their ability to decrease androgen secretion from the ovaries and adrenal glands, reduce 5α-reductase activity, and increase sex hormone–binding globulin.[1,5,7,17,20]

With more than 40 COCs now on the market, choosing the right one for a patient can be daunting.

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There are 3 COCs that have been approved by the US Food and Drug Administration (FDA) to treat acne vulgaris: (1) Ortho Tri-Cyclen®: norgestimate (white tablets, 0.180 mg; light blue tablets, 0.215 mg; blue tablets, 0.250 mg); EE (0.035 mg); (2) Yaz®: DRSP (3 mg) combined with EE (0.02 mg); and (3) Estrostep® Fe: norethindrone acetate (1 mg) combined with EE (white triangular tablets, 20 μg; white square tablets, 30 μg; white round tablets, 35 μg) and ferrous fumarate (75 mg).[21] Because most COCs are effective for most women, drug selection may be more appropriately determined by cost, side-effect profile, lifestyle, and patient preference (Tables 1 and 2). Tolerability of the traditional 7-day placebo hormone-free interval (HFI) plays a critical role. Women who do not have difficulty with this HFI and who are affected by dysmenorrhea and other menstrual irregularities may benefit from traditional, less expensive COCs that simply combine 20 to 50 μg EE and a progestin in a 21 active-tablet and 7 placebo-tablet combination.[21]

Women who experience exaggerated premenstrual symptoms or menstrual headaches during the HFI may be better served by the newest generation of COCs, which have a shorter HFI (Tables 1 and 2). This group of COCs tends to be more expensive than traditional COCs but provides less frequent withdrawal bleeds and similar protection. Specifically, Lybrel® (levonorgestrel [90 μg] combined with EE [20 μg]) entirely eliminates monthly menses and is the first FDA-approved yearlong COC. Yasmin® (DRSP [3 mg] and EE [0.03 mg]) and Yaz are particularly unique because they use antiandrogenic DRSP, a spironolactone analogue, and specifically are marketed to have antiacne effects.[22] Drospirenone is the only FDA-approved progestin with direct androgen receptor–blocking properties.[21] Although the majority of women do well with their first COC, switching drugs occasionally is helpful.[16]

Associated Risks

All COCs have associated risks, but the risks can be minimized with careful patient screening (Tables 3 and 4).[19,23] Although serious adverse events are possible, overall risks for adverse events from COCs are low.[9,19,24-26] Given the low age and generally good health of the patient population for which COCs typically are prescribed, even an elevated relative risk translates into a low absolute risk for notable side effects.[19]

The most substantial risks are cardiovascular.[25] The risk for venous thromboembolism (VTE), deep vein thrombosis, and pulmonary embolism increases with age and is dose related.[9,24] There is a 10-fold increased risk for VTE in the first year and a 2-fold risk in the second year of use and beyond.[26,27] Additionally, there have been concerns that DRSP-containing COCs place patients at a higher risk for VTE compared to traditional COCs, but these concerns have not been supported by more recent studies.[28] Discontinuation of the COC returns a patient to baseline risk within 3 months.[29] Although the risk for VTE while using COCs is widely noted in the literature, the overall risk is relatively low.[9,19]

Myocardial infarction (MI) and ischemic stroke also are rare, even more so than venous events. There is an approximate 2-fold increase in risk for MI and ischemic stroke in women using COCs,[24] but these adverse events are rare in reproductive-aged women, making the incidence low.[9,24] The newer third-generation COCs have no increased risk for MI; some studies even showed a slight reduction in risk.[13,30] However, the risk for MI increases 10-fold in women who smoke and also is higher for women older than 35 years.[24] Guidelines caution physicians against prescribing COCs to women who smoke and are older than 35 years.[13]

The risk for localized breast cancer in patients taking COCs has been debated.[9,19,20,24] One study found a relative risk for breast cancer of 1.24 while taking the drug and an increased risk for up to 4 years following cessation of treatment.[31] However, the risk completely disappeared within 10 years, there was no increased lifetime risk, and the type of cancer was less advanced.[24] None of the data show an increased risk for breast cancer in women aged 35 to 64 years who previously used or currently use COCs.[32] Mortality rates from breast cancer do not increase with the use of COCs.[33]

Combined oral contraceptives only increase the risk for cervical cancer after 5 years of use.[19,24] The risk for cervical cancer immediately begins to decline following cessation of use and is returned to baseline by 10 years.[34] One study found no association between the use of COCs and cervical intraepithelial neoplasia grades 1 or higher among women with human papillomavirus, even beyond 5 years of COC use.[35]

It is important to stress to patients that the risks for COCs have been fairly well elucidated and are substantially less concerning than previously believed if the patient is otherwise healthy.[4] Both patients and physicians may believe that these medications are inherently unsafe,[16,36,37] but these fears are unfounded and contribute to the underutilization of COCs.

Benefits

There also are benefits of COCs that extend beyond their positive effect on acne.[19] Combined oral contraceptives decrease the risk for endometrial and ovarian cancer.[24] This protection continues for at least 20 years following discontinuation of the medication.

Table 1.

Combined Oral Contraceptives (COCs): A Quick Reference

Type/Brand	Active Drugs	Approximate Cost	Miscellaneous
Traditional COCs (21 active tablets; 7 placebo)	EE (20–50 μg); progestin	<$60/mo	
Ortho Tri-Cyclen® (21 active tablets; 7 placebo)	Norgestimate (white tablets, 0.180 mg; light blue tablets, 0.215 mg; blue tablets, 0.250 mg); EE (0.035 mg)	$40/mo	FDA approved for acne vulgaris
Estrostep® Fe (21 active tablets; 7 placebo)	Norethindrone acetate (1 mg); EE (white triangular tablets: 20 μg; white square tablets: 30 μg; white round tablets: 35 μg); ferrous fumarate (75 mg)	$100/mo	FDA approved for acne vulgaris
Yasmin® (21 active tablets; 7 placebo)	DRSP (3 mg); EE (0.03 mg)	$85/mo	Mildly reduces SBP; beneficial for acne, hirsutism, and PCOS
Yaz® (24 active tablets; 4 placebo)	DRSP (3 mg); EE (0.02 mg)	$90/mo	Same as Yasmin; shorter HFI; beneficial for premenstrual dysphoric disorder; FDA approved for acne vulgaris
Loestrin® 24 Fe (24 active tablets; 4 placebo)	Norethindrone acetate (1 mg); EE (20 μg)	$80/mo	Shorter HFI
Seasonale® (84 active tablets; 7 placebo)	Levonorgestrel (0.15 mg); EE (0.03 mg)	$250/mo	Withdrawal bleed every quarter; beneficial for dysmenorrhea, endometriosis, and estrogen withdrawal symptoms
Seasonique® (84 COC tablets; 7 EE-only tablets [0.01 mg]; 0 placebo)	Blue-green tablets: levonorgestrel (0.15 mg) and EE (0.03 mg); yellow tablets: EE (0.01 mg)	$250/mo	Same as Seasonale; shorter HFI than Seasonale
Lybrel® (28 active tablets; 0 placebo)	Levonorgestrel (90 μg); EE (20 μg)	$70/mo	Elimination of monthly menses

Abbreviations: EE, ethinyl estradiol; FDA, US Food and Drug Administration; DRSP, drospirenone; SBP, spontaneous bacterial peritonitis; PCOS, polycystic ovary syndrome; HFI, hormone-free interval.

Data from Spencer et al.[22]

Combined oral contraceptives also may protect women from colorectal cancer.[9,37] Additionally, there is less risk for symptomatic pelvic inflammatory disease, ectopic pregnancy, and benign breast disease, along with improved cycle control, less frequent instances of dysmenorrhea, and increased bone density. Combined oral contraceptives prevent unintended pregnancy, which can pose a substantial health risk, as well as psychologic, social, and financial distress.[9,19,24,25,38]

Table 2.

Choosing an Appropriate Combined Oral Contraceptive (COC)

Clinical Question	Yes	No
Is cost an issue?	Traditional COCs: EE (20–50 μg); progestin	All others: Yasmin® (DRSP, 3 mg; EE, 0.03 mg); Yaz® (DRSP, 3 mg; EE, 0.02 mg); Loestrin® 24 Fe (norethindrone acetate, 1 mg; EE, 20 μg); Seasonale® and Seasonique® (levonorgestrel, 0.15 mg; EE, 0.03 mg)[a]; Lybrel® (levonorgestrel, 90 μg; EE, 20 μg)
Interested in menses elimination?	Total elimination: Lybrel; quarterly menses: Seasonale and Seasonique	Any COC
Are premenstrual symptoms, the HFI, or estrogen withdrawal an issue?	Short HFI drugs: Yaz, Loestrin 24 Fe, Seasonique, +/− Seasonale; no HFI drugs: Lybrel	Any COC

Abbreviations: EE, ethinyl estradiol; DRSP, drospirenone; HFI, hormone-free interval.
[a]Seasonique also has 7 tablets of EE 0.01 mg.

Table 3.

World Health Organization Recommendations for Combined Oral Contraceptive (COC) Usage Eligibility[23]

COC Use Not Recommended	Caution or Special Monitoring
Pregnancy	Breastfeeding (6 wk–6 mo postpartum)
Current breast cancer	Postpartum (<21 d)
Breastfeeding <6 wk postpartum	Age ≥35 y and light smoker (<15 cigarettes per day)
Age ≥35 y and heavy smoker (≥15 cigarettes per day)	History of hypertension (including pregnancy) or if monitoring is not feasible
Hypertension: systolic, ≥160 mm Hg; diastolic, ≥100 mm Hg	Hypertension: systolic, 140–159 mm Hg; diastolic, 90–99 mm Hg; or controlled and monitored
Diabetes with end-organ damage	Headaches: migraine without focal neurologic symptoms <35 y
Diabetes >20 y duration	Known hyperlipidemia should be assessed (eg, type, severity)
History of or current DVT or PE	History of breast cancer with ≥5 y of no disease
Major surgery with prolonged immobilization	Biliary tract disease
Ischemic heart disease (history or current); valvular heart disease with complications	Mild compensated cirrhosis
History of CVA	History of cholestasis related to COC use
Headaches (eg, migraine with focal neurologic symptoms at any age, or without aura if ≥35 y)	Concurrent use of drugs that affect liver enzymes
Active viral hepatitis	
Severe decompensated cirrhosis	
Liver tumor (benign or malignant)	

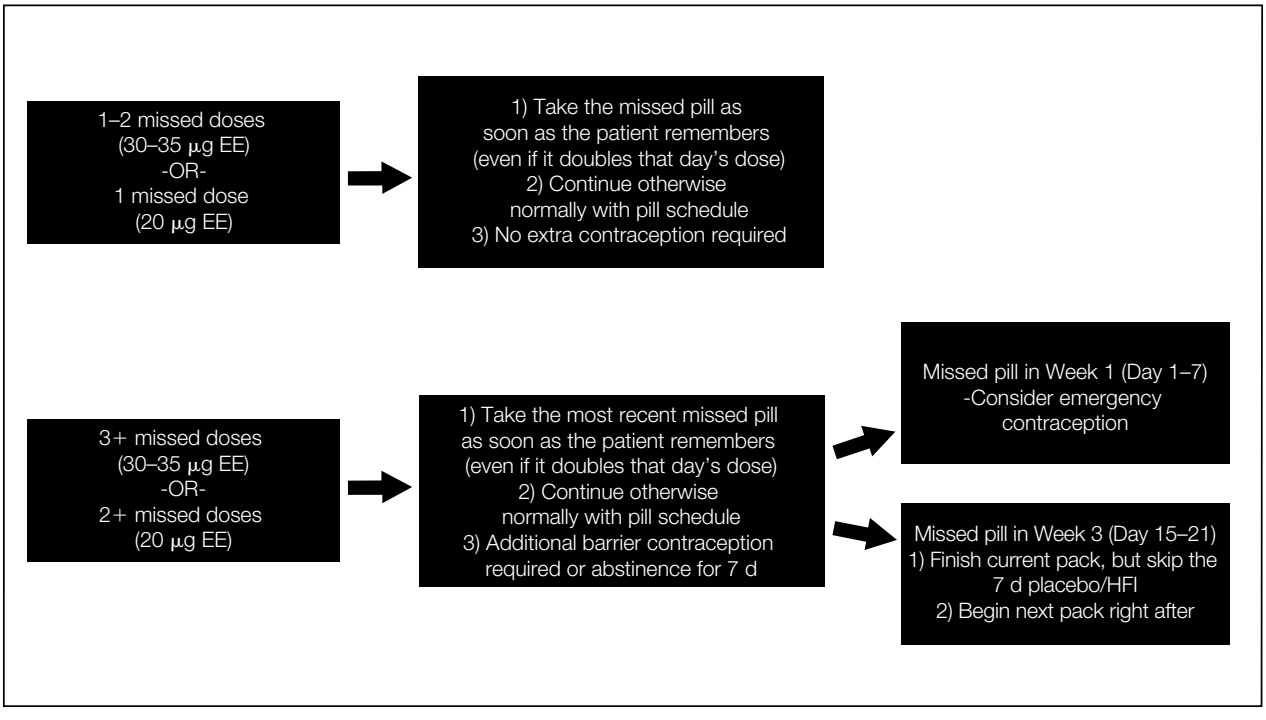
Abbreviations: DVT, deep vein thrombosis; PE, pulmonary embolism; CVA, cerebrovascular accident.

Table 4.

Further World Health Organization Recommendations for Combined Oral Contraceptive Usage: No Restrictions[23]

Postpartum ≥21 d, not breastfeeding	AIDS, HIV infected, or HIV risk
Postabortion	Viral hepatitis carrier
Menarche to age 40 y (nonsmoker)	Uterine fibroids
History of gestational diabetes	History of ectopic pregnancy
Minor surgery without immobilization	Thyroid concerns (goiter, hyperthyroidism, hypothyroidism)
Varicose veins	Thalassemia
Vaginal bleeding (eg, irregular, with or without heavy bleeding after evaluation to exclude pregnancy/malignancy)	Trophoblastic disease (benign or malignant)
Benign breast disease	Iron deficiency anemia
Family history of breast cancer	Epilepsy
Cervical ectropion	Schistosomiasis
Endometrial cancer (while awaiting treatment)	Malaria
Benign ovarian tumor	Antibiotics (concurrent, excluding rifampin and griseofulvin)
Ovarian cancer (while awaiting treatment)	Nulliparous or parous
Pelvic inflammatory disease	Severe dysmenorrhea
Sexually transmitted disease	Tuberculosis
Prior pelvic surgery	Endometriosis
Vaginitis	

Abbreviation: HIV, human immunodeficiency virus.



World Health Organization recommendations for missed doses.[47] EE indicates ethinyl estradiol; HFI, hormone-free interval.

Another benefit of COCs is for women with severe acne who may be future candidates for isotretinoin therapy. In this situation, COCs arguably are the appropriate preceding step, considering the requirement of 2 forms of contraception while taking isotretinoin. By exclusively trying a patient on COCs prior to initiation of isotretinoin therapy, the physician may be better equipped to differentiate the causal medication of mood symptoms, as both medications are cited to produce mood-related side effects.[39,40] In addition, a sufficiently satisfactory response to COCs could occur, which would render treatment with isotretinoin unnecessary.

Initial Evaluation and Monitoring

Initial evaluation should include a measurement of blood pressure and a detailed patient history.[19,23] Physical examination that extends beyond the skin is not necessary or indicated.[16,25,41] Pelvic examination, screening for cervical intraepithelial neoplasia, and breast examination are not required. Although these examinations are valuable as screening tools, they are not helpful in determining which patients should or should not undergo treatment with COCs.[41-44] The American Congress of Obstetricians and Gynecologists guidelines recommend that patients initiate pelvic examination screening at 21 years of age and biennially thereafter, irrespective of the onset of sexual activity or contraception use.[45] Therefore, there is no need for follow-up with a gynecologist after initiation of COCs for acne vulgaris. However, with any medication, return visits to the dermatologist should be scheduled to monitor clinical progress and side effects. Periodic blood pressure measurements also are recommended.[19]

The dermatologist may elect to perform a pregnancy test to enable the patient to start the medication that same day.[16,38] Described as the quick-start approach, beginning to use COCs in the health care provider's office under direct observation has been found to improve short-term compliance compared to initiation after next menses. The rate of pregnancy within the first 6 months of initiation of COCs was lower for those who used the quick-start approach.[46] However, patients must be advised to use a separate method of contraception for the first week to avoid an unintended pregnancy.[16] Alternatively, if the clinician and patient decide to initiate treatment at or immediately after the onset of the next menstrual cycle, a pregnancy test is not needed.[38] The longer the patient delays the initiation of the COC, the less chance she will be adherent.[38,41] No other routine laboratory testing is indicated in an otherwise healthy patient with an unremarkable personal and family history.[16]

Counseling

When prescribing COCs, appropriate counseling regarding when to start is critical. The patient must take the pill each day and be aware of what to do if she skips 1 or more pills (Figure).[47] The chance of pregnancy (1%–3%), the lack of protection against sexually transmitted diseases, and the dangers of concomitant smoking should be discussed.[16,19] Patients should establish a daily routine for taking the COC to maximize compliance.[48] Misconceptions surrounding COCs and pelvic examinations, future fertility or teratogenicity, and risk for weight gain should be dispelled.[16,36,38,49] Finally, the patient should know that it might take several months to see antiacne results,[5,7] and she should not discontinue the medication if it does not work right away. The patient should be given ample time to ask questions and the issues discussed should be documented.

Conclusion

Although some dermatologists may be hesitant to prescribe hormonal therapies, COCs can be safely and appropriately used in eligible female patients with acne. We provided guidelines for the selection of COCs, reviewed the risks and benefits, and described ways to monitor and counsel patients.

REFERENCES

1. Layton AM. A review on the treatment of acne vulgaris. *Int J Clin Pract*. 2006;60:64-72.
2. Tan J. Hormonal treatment of acne: review of current best evidence. *J Cutan Med Surg*. 2004;(8, suppl 4):S11-S15.
3. Helms SE, Bredle DL, Zajic J, et al. Oral contraceptive failure rates and oral antibiotics. *J Am Acad Dermatol*. 1997;36(5, pt 1):705-710.
4. ACOG Committee on Practice Bulletins—Gynecology. ACOG practice bulletin. no. 73: use of hormonal contraception in women with coexisting medical conditions. *Obstet Gynecol*. 2006;107:1453-1472.
5. Katsambas A, Papakonstantinou A. Acne: systemic treatment. *Clin Dermatol*. 2004;22:412-418.
6. Essah PA, Wickham EP 3rd, Nunley JR, et al. Dermatology of androgen-related disorders. *Clin Dermatol*. 2006;24:289-298.
7. Johnson BA, Nunley JR. Use of systemic agents in the treatment of acne vulgaris [published correction in *Am Fam Physician*. 2001;63:following 1295]. *Am Fam Physician*. 2000;62:1823-1830.
8. Golden NH, Carlson JL. The pathophysiology of amenorrhea in the adolescent. *Ann N Y Acad Sci*. 2008;1135:163-178.
9. Burkman R, Schlesselman JJ, Zieman M. Safety concerns and health benefits associated with oral contraception. *Am J Obstet Gynecol*. 2004;190(suppl 4):S5-S22.
10. Lucky AW, Henderson TA, Olson WH, et al. Effectiveness of norgestimate and ethinyl estradiol in treating

moderate acne vulgaris. *J Am Acad Dermatol*. 1997;37 (5, pt 1):746-754.
11. Redmond GP, Olson WH, Lippman JS, et al. Norgestimate and ethinyl estradiol in the treatment of acne vulgaris: a randomized, placebo-controlled trial. *Obstet Gynecol*. 1997;89:615-622.
12. Estrostep Fe [package insert]. Rockaway, NJ: Warner Chilcott US; 2009.
13. Shufelt CL, Bairey Merz CN. Contraceptive hormone use and cardiovascular disease [published correction in *J Am Coll Cardiol*. 2009;53:904]. *J Am Coll Cardiol*. 2009; 53:221-231.
14. Goodman G. Managing acne vulgaris effectively. *Aust Fam Physician*. 2006;35:705-709.
15. Haroun M. Hormonal therapy of acne. *J Cutan Med Surg*. 2004;(8, suppl 4):S6-S10.
16. Rimsza ME. Counseling the adolescent about contraception. *Pediatr Rev*. 2003;24:162-170.
17. Strauss JS, Krowchuk DP, Leyden JJ, et al. Guidelines of care for acne vulgaris management [published online ahead of print February 5, 2007]. *J Am Acad Dermatol*. 2007;56:651-663.
18. Arowojolu AO, Gallo MF, Lopez LM, et al. Combined oral contraceptive pills for treatment of acne. *Cochrane Database Syst Rev*. 2007;1:CD004425.
19. Petitti DB. Clinical practice. combination estrogen-progestin oral contraceptives [published correction in *N Engl J Med*. 2004;350:92]. *N Engl J Med*. 2003;349:1443-1450.
20. Thiboutot D. Acne: hormonal concepts and therapy. *Clin Dermatol*. 2004;22:419-428.
21. Harper JC. Should dermatologists prescribe hormonal contraceptives for acne? *Dermatol Ther*. 2009;22:452-457.
22. Spencer AL, Bonnema R, McNamara MC. Helping women choose appropriate hormonal contraception: update on risks, benefits, and indications. *Am J Med*. 2009;122: 497-506.
23. World Health Organization. *Medical Eligibility Criteria for Contraceptive Use*. 3rd ed. Geneva, Switzerland: World Health Organization; 2004. http://whqlibdoc.who.int/publications /2004/9241562668.pdf. Accessed July 25, 2012.
24. Practice Committee of the American Society for Reproductive Medicine. Hormonal contraception: recent advances and controversies. *Fertil Steril*. 2006;86(5, suppl 1):S229-S235.
25. Deligeoroglou E, Christopoulos P, Creatsas G. Contraception in adolescence. *Ann N Y Acad Sci*. 2006;1092:78-90.
26. Lawrenson R, Farmer R. Venous thromboembolism and combined oral contraceptives: does the type of progestogen make a difference? *Contraception*. 2000;62 (suppl 2):21S-28S.
27. Suissa S, Blais L, Spitzer WO, et al. First-time use of newer oral contraceptives and the risk of venous thromboembolism. *Contraception*. 1997;56:141-146.
28. Tan JK, Ediriweera C. Efficacy and safety of combined ethinyl estradiol/drospirenone oral contraceptives in the treatment of acne. *Int J Womens Health*. 2010;1:213-221.
29. Martinez F, Avecilla A. Combined hormonal contraception and venous thromboembolism. *Eur J Contracept Reprod Health Care*. 2007;12:97-106.
30. Carr BR, Ory H. Estrogen and progestin components of oral contraceptives: relationship to vascular disease. *Contraception*. 1997;55:267-272.
31. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies. Collaborative Group on Hormonal Factors in Breast Cancer. *Lancet*. 1996;347: 1713-1727.
32. Marchbanks PA, McDonald JA, Wilson HG, et al. Oral contraceptives and the risk of breast cancer. *N Engl J Med*. 2002;346:2025-2032.
33. Faculty of Family Planning and Reproductive Health Care, Clinical Effectiveness Unit. FFPRHC Guidance (October 2003): first prescription of combined oral contraception. *J Fam Plann Reprod Health Care*. 2003;29:209-222.
34. Appleby P, Beral V, Berrington de González A, et al. Cervical cancer and hormonal contraceptives: collaborative reanalysis of individual data for 16,573 women with cervical cancer and 35,509 women without cervical cancer from 24 epidemiological studies. *Lancet*. 2007;370: 1609-1621.
35. Harris TG, Miller L, Kulasingam SL, et al. Depot-medroxyprogesterone acetate and combined oral contraceptive use and cervical neoplasia among women with oncogenic human papillomavirus infection. *Am J Obstet Gynecol*. 2009;200:489, e1-e8.
36. Lee J, Jezewski MA. Attitudes toward oral contraceptive use among women of reproductive age: a systematic review. *ANS Adv Nurs Sci*. 2007;30:e85-e103.
37. Fernandez E, La Vecchia C, Balducci A, et al. Oral contraceptives and colorectal cancer risk: a meta-analysis. *Br J Cancer*. 2001;84:722-727.
38. Lesnewski R, Prine L. Initiating hormonal contraception. *Am Fam Physician*. 2006;74:105-112.
39. Segebladh B, Borgström A, Odlind V, et al. Prevalence of psychiatric disorders and premenstrual dysphoric symptoms in patients with experience of adverse mood during treatment with combined oral contraceptives [published online ahead of print September 11, 2008]. *Contraception*. 2009;79:50-55.
40. Brelsford M, Beute TC. Preventing and managing the side effects of isotretinoin. *Semin Cutan Med Surg*. 2008;27: 197-206.
41. Gardner J, Miller L. Promoting the safety and use of hormonal contraceptives. *J Womens Health (Larchmt)*. 2005;14:53-60.
42. Meckstroth KR. Physical examination before initiating hormonal contraception: what is necessary? *Am Fam Physician*. 2006;74:32, 34.
43. Scott A, Glasier AF. Are routine breast and pelvic examinations necessary for women starting combined oral

contraception [published online ahead of print June 10, 2004]? *Hum Reprod Update*. 2004;10:449-452.
44. Stewart FH, Harper CC, Ellertson CE, et al. Clinical breast and pelvic examination requirements for hormonal contraception: current practice vs evidence. *JAMA*. 2001;285:2232-2239.
45. ACOG Committee on Practice Bulletins—Gynecology. ACOG practice bulletin no. 109: cervical cytology screening. *Obstet Gynecol*. 2009;114:1409-1420.
46. Westhoff C, Heartwell S, Edwards S, et al. Initiation of oral contraceptives using a quick start compared with a conventional start: a randomized controlled trial. *Obstet Gynecol*. 2007;109:1270-1276.
47. World Health Organization. *Selected Practice Recommendations for Contraceptive Use*. 2nd ed. Geneva, Switzerland: World Health Organization; 2005.
48. Rosenberg MJ, Burnhill MS, Waugh MS, et al. Compliance and oral contraceptives: a review. *Contraception*. 1995;52:137-141.
49. Cheung E, Free C. Factors influencing young women's decision making regarding hormonal contraceptives: a qualitative study. *Contraception*. 2005;71:426-431.