

Hormonal Contraception

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A. Introduction

The goal of contraceptive therapy should be to not only decrease the rate of unwanted pregnancy but to decrease the incidence of sexually transmitted disease. During counseling sessions with adolescents in particular, remember to discuss both pregnancy prevention and STD prevention. 70% of adolescents have had intercourse prior to the age of 19 and only half used any protection at the time of first coitus. Most adolescents perceive condom usage as pregnancy prevention, not STD prevention. In general, it is wise to recommend both a hormonal contraceptive as well as a barrier method of contraception. New CDC guidelines state spermicide increased risk of STD so emphasize latex.

Oral contraceptives (OC's) are the most popular method of reversible contraception worldwide, particularly among women age 15-29. There are four types of OC's:

1. **Combined, monophasic**-estrogen/progestin formulation does not vary during the cycle
2. **Combined, biphasic**-estrogen/progestin formulation changes at approximately midcycle
3. **Combined, triphasic**- estrogen/progestin formulation changes weekly during the cycle
4. **Progestin-Only**-has no estrogen component

All OC's are highly effective as long as no pills are missed. The provider should select a low dose OC that causes the least amount of side-effects in the user.

B. Components of Combined OC's

Combined OC's consist of an estrogen plus a progestin. The estrogen component in the vast majority of the OC's on the market (and all of the low-dose pills) now consists of the synthetic estrogen, ethinyl estradiol (EE). Several of the newest formulations of oral contraceptives on the market now feature either reduced levels of EE or graduated levels of EE. Other changes in recent formulations of OC's have involved the progestin component. The third generation progestins have higher progestational activity and lower androgenic activity and therefore fewer androgenic side-effects.

Estrogens

Ethinyl estradiol
Mestranol

Progestins**1st Generation**

Norethindrone
Norethynodrel
Ethinodiol diacetate

2nd Generation

Norethindrone acetate
dl-norgestrel
Levonorgestrel

3rd Generation

Desogestrel
Gestodene
Norgestimate

New Class:

Drospironone

USHS FORMULARY : Combined Oral Contraceptives

OC	ESTROGEN	PROGESTIN
Monophasic Pills		
Allesse	20 mcg EE ¹	0.100 mg Levonorgestrel
Ovcon 35	35 mcg	0.4 mg Norethindrone
Loestrin 1.5/30*	30 mcg EE	1.500 mg Norethindrone
Desogen	30 mcg EE	0.150 mg Desogestrel
Multiphasic Pills		
Estrostep*	20 mcg EE	1.00 mg Norethindrone
	30 mcg EE	1.00 mg Norethindrone
	35 mcg EE	1.00 mg Norethindrone
Triphasil	30 mcg EE	0.050 mg Levonorgestrel
	40 mcg EE	0.075 mg Levonorgestrel
	30 mcg EE	0.125 mg Levonorgestrel
OrthoTriCyclen	35 mcg EE	0.180 mg Norgestimate
	35 mcg EE	0.215 mg Norgestimate
	35 mcg EE	0.250 mg Norgestimate
Cyclessa	25 mcg EE	0.100 mg Desogestrel
	25 mcg EE	0.125 mg Desogestrel
	25 mcg EE	0.150 mg Desogestrel
Mircette	20 mcg EE x 21 d	0.150 mg Desogestrel
	Hormone free x 2 d	Hormone free x 2 d
	10 mcg EE x 5 d	No progestin

¹ EE= Ethinyl estradiol

* Being phased out

C. Mechanism of Action of Combined OC's

The progestin component inhibits ovulation by suppressing the release of luteinizing hormone (LH) whereas the estrogen component stabilizes the endometrium and minimizes break-through bleeding. Cervical mucus is also altered as well as the endometrial lining.

D. Differences in Available Combined OC's

1. Differences in progestin component:

As mentioned above, one major difference in available formulations of combined oral contraceptives is the androgenicity of the progestin component. Side-effects of androgenization include:

1. adverse lipid and carbohydrate changes
2. weight gain
3. acne
4. hirsutism
5. mood change
6. nervousness

A practical way of thinking about the different types of combined oral contraceptives is to divide them into categories based on low, medium, and high androgenic activity of their progestin component.

The newest progestin to hit the market is drospirenone, found in the OC *Yasmin* (30 mcg ethinyl estradiol + 3 mg of drospirenone). Drospirenone is an analogue of spironolactone and has antiminerlocorticoid activity. Efficacy is similar to other OC's. Yasmin may be a good choice for women who complain of premenstrual symptoms including water retention. Also, BP actually fell for those treated with Yasmin suggesting that this OC may be a good choice for those women who become hypertensive after starting OCs. The 3 mg of drospirenone in Yasmin is equivalent to 25 micrograms of spironolactone and can cause potassium retention esp in patients also taking potassium-sparing diuretics, ACE inhibitors or angiotensin receptor blockers, other aldosterone antagonists, heparin, or NSAIDs. The potassium level should be checked within a month of starting Yasmin in any patients on these medications. Yasmin is contraindicated in women with renal, hepatic or adrenal insufficiency.

2. Differences in estrogen component:

The 1990's have produced several new formulations of oral contraceptives that alter the estrogen component. All of these pills feature ethinyl estradiol (EE).

The 20 mcg pills are used largely for women who have estrogen-related side-effects such as nausea, breast tenderness, and vascular headaches. Their major disadvantage is spotting and a smaller margin of error for late or missed pills.

3. Differences in hormone-free interval:

One of the latest oral contraceptive formulation changes is to alter the hormone-free interval. Many clinicians believe that the relatively long 7-day hormone-free interval is the source of much of the unwanted spotting and break-through bleeding as well as the source of break-through pregnancies. The makers of Mircette addressed this by giving only 2 hormone-free days and supplying a low dose of EE during the other 5 days. It is thought that this low dose EE (10 mcg) suppresses the action of FSH on follicle development.

OC With Shortened Hormone-Free Interval

OC	Days	Estrogen	Progestin
Mircette	21	20 mcg EE	150 mcg desogestrel
	2	Hormone-free	Hormone-free
	5	10 mcg EE	No progestin

4. Differences in prescribing of oral contraceptives:

A final change which has been around for a long time but which is being more vigorously promoted is a change in the way oral contraceptives may be taken. “Tricycling” refers to taking 3 or 4 packs of oral contraceptives in a row without taking the placebo pills. At the end of the third or fourth pack, the woman does not take any pills for 4 days. She then resumes “tricycling”. This method is useful for women who have had refractory break-through-bleeding or who are on anti-convulsants or who experience vascular HA during the hormone-free period. It is also useful for those women who do not want to have menses!

5. On the Horizon:

Seasonale is a 90 day cycle OC. The advantage here is only 4 periods per year (going back to the women of a century ago who only had 40-50 periods in their lifetime). Main side effect was increased breakthrough bleeding.

E. Noncontraceptive Benefits of Combined OC's

Tailoring the message about the noncontraceptive benefits of OC's to the age-group may be helpful in promoting the use of OC's. The teenager may be more interested in decreasing menstrual cramps and the older woman more interested in reduction in the incidence of ovarian and endometrial cancer. Combined OC's:

- Improve acne
- Minimize menstrual cramps
- Decrease menstrual bleeding
- Reduce incidence of iron deficiency anemia
- Decrease PMS symptoms
- Increase menstrual cycle regularity

- Protect against Pelvic Inflammatory Disease
- Protect against ovarian and endometrial cancer
- Decrease the incidence of fibroids and ovarian cysts
- Decrease the incidence of benign breast disease
- Prevent ectopic pregnancy
- Ability to use pills as emergency contraception
- Improve symptoms of endometriosis
- Other possible benefits include: prevention of rheumatoid arthritis and increased bone density

F. Patient Evaluation and Prescribing

It is acceptable to start OC's and then perform Pap testing within 3-6 months. It is acceptable to prescribe OC's to a young teenager who has never been sexually active without a Pap smear if the pills are warranted to control heavy menses, menstrual cramps or acne etc. New guidelines per American Cancer Society report cervical cancer screening should begin 3 years after woman becomes sexually active but no later than 21 years old.

G. Contraindications to Prescribing Combined OC's

Nearly all excess mortality in OC users is due to circulatory disease (DVT or PE, HTN, MI or CVA). The risk of circulatory death increases with the dose of estrogen, age, smoking or another cardiovascular risk factor such as hyperlipidemia, diabetes, or HTN.

All women who use OC's should be strongly advised not to smoke and OC's should not be prescribed to women over the age of 35 who smoke. It is not necessary to check a lipid profile prior to prescribing OC's as the low dose formulations that are most widely used have no adverse impact on the lipid profile except for a moderate increase in triglycerides. In women >40 with a family history of hypertriglyceridemia, AODM or CAD, a lipid screen may be prudent.

You should at least take a family history of clotting events or disorders. Activated Protein C Resistance (APCR) is a common (5% of the population), and is an autosomal dominant mutation in Factor V, which increases the likelihood of clotting. 20-40% of patients with a venous thromboembolism have APCR and will often have a family history of DVT. Individuals with a positive family history should be screened for APCR before starting OC's. See table on p 11 of this handout: the incidence of venous thromboembolism in women with the Factor V Leiden mutation on OCs is 19-28.5/10,000 woman-years compared to 0.8/10,000 woman-years in premenopausal women without the mutation and not taking OCs.

Absolute contraindications for combined OC's include:

- Active thrombophlebitis or history of thromboembolism
- Hypercoagulable states
- Cerebrovascular disease
- Coronary artery disease

- Presence or personal history of breast cancer (not family history)
- Endometrial cancer
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy
- Jaundice with prior OC use
- Hepatic adenomas or carcinomas
- Pregnancy
- Complicated migraines

Strong relative contraindications to OC's include:

- Severe headache induced by OC's
- OC induced HTN (some practitioners treat the HTN and continue the OC's)
- >40 with a second circulatory risk factor
- >35 and a smoker

Long-Term Safety of Oral Contraceptives:

The long-term safety of combined oral contraceptives (largely OC's containing 50 mcg estrogen) has been confirmed by a large cohort study from the Royal College of General Practitioners in Great Britain. This study was published in January, 1999 in the *British Medical Journal*. They followed 46,000 women, half who were using oral contraceptives at recruitment. Relative risk of death adjusted for age, parity, social class and smoking revealed that risk of death from all causes was similar in ever users and never users of oral contraceptives. However, among current or recent users (within 10 years), there was a protective effect against ovarian CA (RR 0.2) but an increased risk of death from cervical CA (RR 2.5) and from CVA (RR 1.9). Death from thromboembolic events was not separated out from death from other circulatory causes. Death from breast cancer was slightly higher during use and for the 10 yrs after stopping use but there was no excess risk 10 or more years after stopping.

H. Starting Combined OC's

Selection of an OC for a particular patient depends upon the patient's characteristics to some extent but largely upon the clinical experience of the provider with various formulations! Pick a limited set of different OC's and become familiar with using them. Encourage the patient to stay on the OC for at least 3 cycles as most minor side-effects disappear within 3 cycles. If you decide to switch OC's at the end of the 3rd cycle, pick an OC with a different progestin rather than an OC containing a different dose of the same progestin.

In USHS, we bring the new starts back in 3-4 months to monitor blood pressure and any persistent side-effects.

1. For New Starts:

- Pick a 35 mcg (or lower) estrogen OC. Third generation progestin-containing OCs have a lower incidence of androgenic side-effects and at least as good cycle control as older preparations; however, controversy remains regarding whether these formulations increase the risk of venous thromboembolic disease (see page 8-9 of this handout) over older preparations.
- Both monophasics and triphasics work well and have high patient satisfaction but it is easier to counsel a patient who has missed pills if they are taking a monophasic.

2. For Continuing Patients on a 35 mcg (or lower) Estrogen Preparation:

- If the patient is doing well on their current OC, continue it.

3. For Continuing Patients on a 50 mcg Estrogen Preparation:

- Switch to a 35 mcg estrogen or lower OC. 35 mcg preparations are less thrombogenic.

4. Reserve 50 mcg Preparations for patients who:

- Take anticonvulsants
- Have intractable BTB; the provider may be able to manage these patients with a short-term course of 50 mcg
- Have persistent functional ovarian cysts

5. For Post-Partum Women:

- Begin a 20-35 mcg estrogen OC on the second or third Sunday after delivery for nonlactating women. The Health Dept starts women on the first Sunday after delivery.
- For lactating women who regularly breastfeed every 4 hours and do not supplement, there is no need to worry about pregnancy for at least 2-3 months. If the patient wishes to start something, use a progestin-only OC beginning 6 weeks after delivery and continuing until supplemental feeding begins. At that point, switching to a combined OC is appropriate. Estrogen containing preparations decrease milk production.

I. Managing Side-Effects of Combined OC's

1. Breakthrough Bleeding:

- Wait three cycles; in most cases, BTB will disappear
- Make sure the patient is taking the OC at the same time every day.
- Has another medication been added? (antibiotic, rifampin, seizure meds?)
- Is the patient a smoker? Encourage her to stop.
- Rule out infection; chlamydial cervicitis is high among OC users reporting BTB
- If incorrect use and infection have been ruled out, try switching to a different progestin
- If BTB persist on the new progestin, try increasing the estrogen dose to a 50 mcg pill or add 20 mcg ethinyl estradiol daily, or 0.625 mg conjugated estrogen daily, or 1 mg or 2 mg estrace daily for a few months.
- Investigate the possibility of a polyp or a submucosal fibroid (typically these cause irregular bleeding without regard to the time in the OC cycle)

- Vitamin C at 500-1000 mg/d has been reported to increase estrogen levels by up to 50% so this may be an option
- If all else fails, try Mircette or “tricycle” the patient.

2. **Weight Gain:**

- It’s probably not due to the Pill! The maximum mean weight gain after one year of use in clinical studies of norgestimate or desogestrel OC’s was ½ lb!

3. **Headache:**

- Check BP.
- Try a 20 mcg pill.
- If the patient is using an older preparation, switch to a norgestimate or desogestrel containing OC. If there is no improvement or worsening, select another method of contraception.
- If headaches consistently occur in the pill-free interval, the HA most likely represents an estrogen-withdrawal HA. Try “tricycling” or Mircette.
- If the patient develops migraines, see discussion below

4. **Mood Change:**

- Low dose OC’s rarely affect mood. If the patient complains of mood changes, switch to an OC with a different progestin.
- Alternatively, irritability during OC use or after OC discontinuation may be due to vitamin B6 deficiency. Consider supplementing with 50mg of vitamin B6.

5. **Nausea:**

- Should resolve in 3 cycles.
- Take the OC with meals.
- Try taking OC in the evening.
- Switch to a 20 mcg estrogen preparation (Alesse, Levlite).

6. **Breast Tenderness:**

- Should resolve in 3 cycles.
- Check pregnancy test if persistent.
- Do breast examination to assure that no lumps are present.
- Avoid caffeine, chocolate.
- Add Vitamin E, 400 IU bid
- Switch to a 20 mcg estrogen preparation (Alesse, Levlite).

7. **Cancer Associates**

- Ovarian cancer decreased by 30% after 4 years on OC
- Endometrial cancer decreased by 40% after 2 years on OC
- Breast cancer risk is controversial

- Data from 54 epidemiological studies showed a slight risk of breast cancer among current users. There was no increased risk after women had stopped OC for 10 years or more.²
- A case-control study of over 9000 women showed no excess risk in current or former OC users even if they had a family history of breast cancer.³

Comment:

8. Adverse Lipid Effects:

- Older preparations like Ovral may decrease HDL and raise LDL; that this may be clinically significant is not proven. However, Ovral is no longer used as an OC.
- All combination OC's increase triglyceride levels largely because of their estrogen component. However, norgestimate compounds increase triglyceride levels less than desogestrel compounds. You can also try the 20 mcg pills. If the triglyceride level is >350, switching to a progestin-only pill is prudent.

9. Glucose Intolerance:

- Older, high-dose OC's were associated with an abnormal glucose-tolerance test; no low-dose pill has any measurable effect on carbohydrate metabolism

10. Thrombotic Effects:

- Thrombotic effects are primarily related to the dose of the estrogen component; in general, there is a decreased risk associated with decreasing estrogen dose. However, there is no known significant difference in risk with a 20 mcg vs a 30 or 35 mcg estrogen preparation, even among smokers.
- Stop any OC the month before elective surgery that will result in immobilization or in the case of trauma that results in immobilization.
- **Do OC's containing third generation progestins (norgestimate, desogestrel or gestodene [not available in the US]) increase the risk of thromboembolism?** Several epidemiologic studies have reported a possible association of these OC's with a 1.5-2.0 increased risk for venous thromboembolism. Some experts feel that this risk is not real:
 1. There is no logic to the association. Given our knowledge about how estrogen affects the coagulation system, it is not biologically plausible that the progestin component of an OC should impact the risk of thromboembolism. Also, some of the studies have shown a decreased risk for MI in women on these agents.³ Also, norgestimate (which is metabolized to levonorgestrel, a 2nd generation progestin that has not been associated with increased risk of venous thromboembolisms and which has been around for a long time) shows an increased risk.
 2. Patients who present with symptoms on the newer agents are subjected to more aggressive evaluation than in the past.

² Collaborative Group on Hormonal Factors in Breast Cancer. 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. *Lancet* 1996;347:1713-1727.

³ National Institute of Child Health and Human Development Women's Contraceptive and Reproductive Expenses (Care) study. Oral Contraceptives and the Risk of Breast Cancer *NEJM* 2002;346:2025-2032.

3. Patients with subtle risk factors may be more likely to receive the newer agents because clinicians may perceive that “newer” is safer or better; therefore, desogestrel or gestodene containing OC’s may be prescribed more frequently to users with increased risks for venous thromboembolism.
- The FDA concluded in a letter to US clinicians that the additional risk of DVT due to use of third-generation OC’s “is not great enough to justify switching to other products.”¹
 - Many prescribers feel entirely comfortable that desogestrel (and gestodene) containing OC’s are perfectly safe.
 - Other prescribers adopt a compromise approach: If patients are on desogestrel containing OC’s, counsel them regarding the current studies. If they are doing well on desogestrel containing OC’s, it is OK to continue this formulation. If they are obese or have severe varicose veins, you may consider switching them to another formulation. For new starts, pick a second-generation agent (levonorgestrel or dl-norgestrel or norethindrone).²

Incidence of Venous Thromboembolism with Oral Contraceptive Use¹

Population and Type of OC	Incidence per 10,000 woman-years
Premenopausal woman not taking OC’s	0.8
Women taking any combined OC	3-4
Second-generation progestins	
Monophasic levonorgestrel	2.5
Others (not levonorgestrel)	1.8
Third-generation progestins	
Desogestrel + 30 mcg EE	4.0
Gestodene	4.4
Pregnant women	6.0
Women with Factor V Leiden mutation	
Not taking OC’s	5.7
Taking OC’s	19-28.5

¹ Adapted from Qureshi M and Attaran M, Review of newer contraceptive agents, Cleveland Clinic Journal of Medicine 1999; 66:358-366.

- **Does the risk of myocardial infarction differ with varying types of oral contraceptives?** In a case-control study of 248 women aged 18-49, the odds ratio of having an MI was 2.5 for women using an OC with a 2nd generation progestin (levonorgestrel) compared to an OC with a third generation progestin (desogestrel or gestodene).³ However, another case-control study showed no association between type of OC formulation and risk of MI among OC users.⁴

¹ Food and Drug Administration, Oral contraceptives and risk of blood clots. FDA Talk Papers, Nov. 14, 1995.

² Vendenbroucke JP, et al. Oral contraceptives and the risk of venous thrombosis. NEJM, 2001; 344:1527-1535.

³ Tanis BC, et al. Oral contraceptives and the risk of myocardial infarction. NEJM, 2001; 345:1787-1842

⁴ Rosenberg L. Low-dose oral contraceptive use and the risk of myocardial infarction. Arch Intern Med, 2001;161:1065-1070.

11. Amenorrhea

- Missed pills or late pills may increase the risk of pregnancy; check a pregnancy test. If pregnant, stop OC's (can counsel patient that there will be no harmful effects on the fetus)
- Patients on 21 day packs may forget to leave a pill-free week.
- If the pregnancy test is negative, amenorrhea on a 20-35 mcg estrogen OC is secondary to lack of endometrial lining build-up. Reassure the patient that this is not harmful.
- If on a 20 mcg pill, can increase to a 30-35 mcg pill.
- Amenorrhea may develop after the patient has been on OC's continuously for a long period of time; again, this is not harmful but rather due to lack of endometrial lining build-up.
- If the patient is uncomfortable having no menses, you may do one of the following:
 1. Stop OC's and allow endometrial lining to regenerate (use another form of contraception.
 2. Switch to a higher estrogen OC for 3 months.
 3. Add 20 mcg ethinyl estradiol daily for 3 months.

12. Hypertension

- If the patient develops hypertension while on OC's, you may either select another method (Yasmin may be an option) or continue OC's and Rx the HTN. If the patient has an additional circulatory risk factor in addition to HTN, the better choice would be to discontinue OC's.

13. Hepatocellular adenoma:

- Rare Benign liver tumors have been associated with use of combined pills. Although histologically benign, they may grow, rupture through the capsule, cause extensive bleeding, even death. Abdominal pain may continue for months before this tumor is diagnosed. OC's should be discontinued.

J. Prescribing Combined OC's in Women with Medical Conditions

Certain medical conditions may influence your choice of OC.

1. Acne:

- Pick a norgestimate or desogestrel containing OC; OrthoTriCyclen is marketed specifically for improving acne
- OC's with low dose norethindrone (0.4-0.5 mg) may also be acceptable.

2. Hirsutism:

- Pick a norgestimate or desogestrel containing OC.
- OC's with low dose norethindrone (0.4 mg) have been as effective as spironolactone in inhibiting excessive hair growth.

3. Obesity:

- Obese women with acne and hirsutism often have Polycystic Ovarian Syndrome and will benefit from a norgestimate or desogestrel containing OC. See chapter on PCOS as there are other treatments for PCOS besides OC's.
- Efficacy of the OC is not affected by weight.
- Very obese women may have high triglycerides that could be exacerbated by OC use.

4. Hypertension:

- A history of pregnancy-associated HTN is not a contraindication to use of OC's. Wait 4-6 weeks post-delivery; if BP has returned to normal, you may try OC's with monitoring.
- OC's may be used in women age 35 or younger with well-controlled HTN provided they are otherwise healthy, nonsmokers, and have no evidence of end-organ disease; use an OC with <35 mcg estrogen and monitor carefully.
- Progestin-only methods can be used in women with HTN who are older than 35
- Avoid OC's in patients with HTN and collagen vascular disease as HTN is often difficult to control in such patients.

5. Dyslipidemias:

- If elevated cholesterol is the only circulatory risk factor, low androgenic OC's are acceptable.
- Lower estrogen dose pills exacerbate triglyceridemia less than higher estrogen pills. You can try a 20 mcg pill.
- If the patient has a triglyceride > 350, estrogen-containing OC's should be avoided.
- Norgestimate containing OC's increase triglycerides less than do desogestrel or gestodene OC's.

6. FH of Premature CAD:

- Patients with low HDL's and high LDL's may actually have their lipid panels improve on low androgenic OC's. However, if age >40, HTN, AODM or smoking are other risk factors, avoid combined OC's.

7. Patients with CAD, CHF, or CVA:

- Progestin-only contraceptives may be appropriate here; never combined OC's

8. Cigarette Smoking:

- Encourage all smokers to stop.
- Do not prescribe OC's to smokers > age 35. ACOG concurs.
- Smokers between the ages of 30-35 should receive OC's with ≤ 35 mcg estrogen. ACOG does not address this group.

9. Diabetes/Gestational Diabetes:

- Select a low androgenic progestin OC with less than 35 mcg of estrogen
- Use only in diabetic women less than the age of 35 who are otherwise healthy with no evidence of HTN, nephropathy, retinopathy or other vascular disease.

- Progestin-only methods can be used in women with diabetes with vascular disease or older than 35

10. Family History of Breast Cancer:

- Data suggest that it is safe to prescribe OC's to patients with a FH of breast cancer; the American College of Obstetricians and Gynecologists (ACOG) agrees

11. Benign Breast Disease:

- Data from studies with older preparations suggest a decrease in incidence of benign breast disease with OC use; there is no data yet on the newer preparations. ACOG agrees with prescribing OCs to pts with fibroadenoma or other benign breast disease

12. Migraine:

- ACOG recommends a progestin-only method for patients with migraines.
- Migraine is very common in the reproductive age group (20% of women). If OC use worsens the headaches, they should be stopped.
- If you are going to try an OC in a patient with migraines, it makes more sense to select a monophasic preparation as migraine headaches are known to be associated with *changes* in hormone levels.
- WHO recommends not using OC in women with migrains who are 35 years or older.
- If HA episodes include focal neurologic symptoms (scotoma, paresthesias, vertigo or seizures,etc), than OCP's are contraindicated.
- See previous discussion under "Managing Side-Effects" for advice about HA.

13. Depression:

- There is no evidence that different OC's have different effects in women with depression.
- OC's are more readily discontinued in the event of worsening depression than is DepoProvera.

14. Misc:

- Progestin-only methods may be safer for women with lupus or sickle-cell anemia although the WHO consensus panel states that the benefits of OC's in sicklers outweigh the risks

K. Selecting Combined OC's for Therapeutic Uses

Combined OC's may be used to treat various gynecologic conditions.

1. Dysfunctional Uterine Bleeding (DUB):

- Ovulatory DUB is common in women of all ages and is characterized by menorrhagia (prolonged or excessive menstruation).
 1. In teenagers, R/O coagulation disorders before prescribing OC's to control menorrhagia
 2. In women > 35, R/O endometrial polyps or fibroids before prescribing OC's to control bleeding.

3. Use a monophasic levonorgestrel containing OC (Nordette or Levlen), especially if bleeding is severe (androgenic progestin shuts down the endometrium)
4. Continuous use of a NSAIA during menses will decrease flow.

- Metrorrhagia (intermenstrual bleeding) may be managed with an OC that offers superior cycle control, again a levonorgestrel formulation for maximum suppression of endometrial growth (unless the patient already has signs of hyperandrogenism).

2. Persistent Anovulation:

- Hyperandrogenic chronic anovulation (PCO) is managed with an OC containing a low androgenic progestin. Alternatively, one can use a 0.4-0.5 mg norethindrone-containing preparation.

3. Ovarian Failure:

- The average age of menopause is 51.4 years.
- In perimenopause, there may be periodic ovulatory cycles with potential fertility.
- Use of OC's in the healthy, nonsmoking 40-50 year old patient with declining ovarian function or in the nonsmoking woman in her 30's with premature ovarian failure can prevent pregnancy, regulate the menstrual cycle, prevent ovarian and endometrial cancer, and probably reduce bone loss. Pick a low androgenic progestin-containing OC.
- Continue OC's until age 50. Measure FSH in the 6th or 7th hormone-free day. If FSH > 25 mIU/ml, you may switch to HRT if the patient desires medication for hot flashes. If menstrual irregularity occurs after the switch, put her back on OC's for another year and try again.
- Alternatively, continue OC's until age 50, then stop OC's. If menses stop, can switch to HRT if patient so desires. If menses resume, discuss with patient whether she wants to continue on OC's for another year or two.

4. Dysmenorrhea:

- OC's decrease primary dysmenorrhea (related to ovulatory cycles) by inhibiting ovulation, suppressing prostaglandin production and producing a thinner endometrial lining.
- Advise use of a NSAIA on a regular basis throughout the menses.
- If the low androgenic formulation does not decrease dysmenorrhea sufficiently, try a monophasic levonorgestrel-containing pill to suppress the endometrium

5. Mittelschmerz

- All OC's will eliminate this pain of ovulation; no one formulation is better than another

6. Endometriosis

- OC's suppress growth of endometrial implants and are favored over danazol and gonadotropin-releasing hormone (GnRH) agonists as these latter are more expensive and are more likely to cause side-effects.
- Pick a medium androgenic progestin formulation (0.15 mg levonorgestrel or 0.3 mg norgestrel with 30 mcg estrogen) used continuously without a pill-free interval until the

pain disappears (up to nine months). If BTB occurs, the pt can go off continuous active pills, have a withdrawal bleed, and then restart the continuous regimen.

7. Functional Ovarian Cysts

- Common in reproductive age women, usually disappear spontaneously
- May cause significant pain; can rupture and cause intraabdominal bleeding
- Torsion requires surgical intervention
- Monophasic OC's > 35 mcg estrogen work best to suppress ovarian cyst formation but probably dose of estrogen is more important than the estrogen regimen.

8. Control of Menstrual Bleeding in the Presence of Blood Dyscrasias

- ITP may cause such heavy menses that transfusion is required.
- Continuous OC's for 6-9 months may be useful in preventing withdrawal bleeding.

9. Emergency Contraception

- Used to prevent conception from unprotected intercourse which occurred in the 72 hours prior to beginning medication
- 75-80% effective at preventing pregnancy.
- Common side-effects are nausea (you may wish to give her a prescription for compazine), spotting/bleeding. Nausea is less of a problem with Plan B.

1. OCs that can be used for emergency contraception need at least 100 micrograms of EE and either 100 mg of norgestrel or 50 mg of levonorgestrel. If using 30-35 mcg estrogen OC (Nordette, Levlen, Lo/Ovral) : Take four 30-35 mcg pills as soon as possible after intercourse followed by four 30-35 mcg pills 12 hours after the first dose. If using Triphasil or Tri-Levlen, make sure the pills taken are the yellow pills. If using Alesse or Levlite, take 5 pills with each dose.
2. You may prescribe the Preven kit which contains a urine hCG test, and 4 doses 50 mcg EE/0.25 mg levonorgestrel. The patient assures she is not already pregnant by obtaining a negative urine hCG, then takes 2 doses of the light blue pills followed in 12 hours by the second 2 doses. This kit is marketed for phone-in prescribing. No office visit is required.
3. Plan B consists of two doses of 0.75 mg levonorgestrel taken 12 hrs apart.
4. Remember the need to start contraception. Patient should return if no menses in three weeks.

L. Drug Interactions with Combined OC's

Antibiotics which have definitely been shown to reduce OC effectiveness include rifampin , griseofulvin, and possibly some rarely used antiparasitics. It is controversial whether broad-spectrum antibiotics such as ampicillin or tetracycline contribute to OC failure. A possible mechanism for this interaction is a decrease in gut flora thereby decreasing the reabsorption of estrogen in the gut. USHS recommends a back-up method of contraception during antibiotic use.

OC's should not be used with carbamazepine (Tegretol), phenytoin (Dilantin), primidone, or barbiturates (phenobarbital and others) as these drugs decrease OC effectiveness. Patients with seizure disorders should select another method of contraception. Some clinicians manage these patients on 50 mcg pills or by "tricycling."

OC's increase the effect of theophylline and theophylline levels should be monitored in OC users on this drug.

M. Pearls of Wisdom

- 1. How to take the Pill:** Begin the first pill on the Sunday after your period begins. If your period begins on a Sunday, take your first pill that same Sunday. Try to take the Pill at the same time every day.
- 2. How to delay bleeding (vacation, honeymoon, etc):** Do not take the hormone free pills. Immediately begin a new pack of pills on the 22nd day of the pack.
- 3. How to manage missed pills:**
 1. One missed pill: Take two pills at the next scheduled time and complete the pack as usual.
 2. Two consecutive missed pills: Take two pills immediately. Take 2 pills the next day and then 1 pill daily for the rest of the pack. Use a backup method the remainder of the cycle.
 3. More than two consecutive missed pills: Consult the package insert (instructions will vary depending upon whether the OC is monophasic or multi-phasic).
- 4. After how long should a woman on combined OC's be encouraged to take a break from them?** This practice is discouraged whether the woman has been on them 10 or 20 years. Some argue that a woman who has been on OC's for 10 years has been off of them for 1 week out of every 4 so in 10 years she has been off them 2 1/2 years!

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