2010

Contraception

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In: Pediatric and Adolescent Sexuality... ISBN: 978-1-60876-735-9
Ed: H. A. Omar et al.

Chapter 8

CONTRACEPTION

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Contraception is an important concept for sexually active adolescent females to understand who do not wish to become pregnant. This chapter reviews important, effective, and safe contraceptive methods that can be used by female youth. These methods include abstinence, oral contraception, contraceptive patch.

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mini-pills, emergency contraceptives, injectable contraception (DMPA). implants (lmplanon), intravaginal ring, vaginal barrier contraceptives, intrauterine devices, and natural family planning. Promotion of se1rnal responsibility should be the charge of health professionals caring for adolescents and young adults.

INTRODUCTION

An important issue for human beings is the acquisition of normal sexual healtl1, including the understanding and application of reproductive health when needed (1-5). Unfortunately, comprehensive sexuality education is not a topic provided to many of our children, adolescents or college students in the United States (5). The median age at first intercourse of 16 years in the United States is comparable to the age of coital initiation in other developed countries such as Canada, countries of Western Europe (France, Great Britain), countries of Eastern Europe and Eurasia (Russia) (6-11).

Students who were sexually active in high school may continue to be at risk for pregnancy and sexually transmitted diseases in their college life; those youth who chose abstinence at one point may abandon this concept as they mature, choosing coital behavior with one or more partners in junior high school, high school, or college (8,12-14). There are over 15 million cases of sexually transmitted diseases in the United States, and over 60% of these occur in young people under 25 years of age) (4,7).

All youth who are sexually active, including those with chronic illness, should be provided with appropriate contraceptive counselling and contraceptive prescription if they are not willing to accept abstinence (1,2,15-17). Since millions of female adolescents are sexually active, it is important that clinicians caring for them provide appropriate sexuality counselling, covering such topics as safe sex. contraception, and STD/AIDS prevention (12,18-21). Reasons for not using contraception include being abstinent, wishing to become pregnant, concluding they or their partners were sterile, fear of contraceptive *"side effects"* (such as breast cancer or gain), religious objections regarding contraception, lack of clinician education about contraceptives, history of

contraception or abortion, failure of insurance to cover contraception, and others (1,2,22-27). Approximately half of adolescent pregnancies occur within the first six months after the initiation of coital behaviour, while adolescents wait one year or more after starting coitus to seek advice from clinicians about effective contraception. Higher socioeconomic status and education are factors that lead to an increase in delay in coitus and willingness to use effective contraption if sexually active (28). Although adolescent pregnancy rates have dropped 33% in the United Sates from the early 1990s to 2003, the rates in the U.S. are the highest in developed countries with a birth rate in 15 to 19 year olds at 41.7/1 ,000 (14,29).

A number of safe and effective contraceptive methods are available (1-4,15,18,20,30,31) (see table 1). The gap between efficacy of perfect use of contraceptives (e.g., correct, consistent, and continued use of a chosen contraceptive method) and typical use leads to millions of unintended pregnancies each year (1,2,4,32-36). Efficacy rates of contraceptives are noted in table 2 (35,36). The barrier methods (i.e., condoms, diaphragms, cervical caps, vaginal sponges, female condoms, and vaginal spermicides) can be used quite effectively by motivated high school or college students who are taught how to use them; periodic abstinence has higher pregnancy rates, but is potentially an effective contraceptive method. The female's comfort for insertion of barrier methods is crucial for maximum contraceptive efficacy for these methods, and thus, they are not appropriate for many adolescent who do not have this comfort level.

Norplant, an effective method in which six progesterone capsules are inserted subcutaneously into the upper arm, was removed from the United States market in 2000. Implanon, a single progesterone rod implant, has now replaced Norplant in the Uniled States. The intrauterine device is an excellent contraceptive, but has been tainted with the image of inducing pelvic inflammatory disease (1,37). These contraceptive methods are discussed later in this discussion.

Table 1. Contraceptive methods

Abstinence
Combined Oral Contraceptives (COCs)
Contraceptive patch
Mini-pills (Progestin-only pills; POPs)
Emergency contraceptives
Injectable Contraceptives
Depo-Provera® (Depo-medroxy-progesterone acetate
Lunelle® (estradiol cypionate and medroxyprogesterone acetate)
Implants
Norplant I (withdrawn from the US market in 2000)
Implanon (one rod system with etonogestrel)
Jadelle (Norplant II: two silastic rods with levonorgestrel)
Intravaginal ring (NuvaRing)
Intrauterine Devices
Progestasert® IUD (with progesterone)
ParaGard® (Copper T380A IUD)
Mirena® (IUD with levonorgestrel)
Vaginal barrier contraceptives
Cervical cap (Prentif Cavity-rim®)
Condoms (male)
Contraceptive sponge (vaginal)
Diaphragm
Female condom (Reality®)
Spermicides (vaginal)
Sterilization (female sterilization, vasectomy)
Physiological methods/natural family planning
Coitus interruptus

Table 2. Efficacy of contraceptives (40,41)

Contraceptive Efficacy	First Year Failure Rate	
	Typical Use	Perfect Use
Combined OCs	3-8	0:1
Progesterone IUD	2	1.5
Copper T IUD	0.8	0.6
Mirena IUD	0.2	0.1
DMPA	0.3	0.3
Norplant	0.05	0.05

The choice of currently available contraceptive methods has increased considerably in recent years, offering females of reproductive age a variety of different methods that retlect their various needs and lifestyles. A number of contraceptive methods have received United States Food and Drug Administration (FDA) approval over the past two decades (see table 3), including emergency contraceptives (Preven, Plan B), Depo-Provera (DMPA), the cervical cap, Lunelle (injectable contraceptive with estrogen), Mirena (an IUD with levonorgestrel), a contraceptive patch (Evra), an intravaginal ring (NuvaRing), and implants such as Implanon (28,38-40).

Table 3. FDA approval history for contraceptives

1. 12/90: Norplant (Withdrawn from US Market in 2000)
2. 10/92: Depo-Provera
3. 9/98: Preven Kit
4. 7/99: Plan B
5. 10/00: Lunelle, "injectable pill" (withdrawn from the US Market)
6. 12/00: Mirena IUD
7. 10/01: Nuva Ring (vaginal ring)
8. 11/0l: Evra Patch
9. 2006 Implanon (single rod)

Technology has expanded over the past decade to include various ways of contraceptive steroid release (see table 4), leading to a number of potential advantages (see table 5). After OCPs were developed over 45 years ago, the emphasis has been on having newer pill formulations with lower doses of estrogens as well as various progestins and developing phasic dosing regimens. Recently, newer delivery systems of hormones have been developed to help decrease contraceptive failure rates associated with incorrect use of contraceptives. For example, the patch and ring are user controlled and easy to discontinue. thus, being more appealing to some females (seetable4) (15,41).

Table 4. Methods to deliver steroids

Pills
Patch
Injectables
Hormone-releasing IUDs
Implants
Vaginal rings

Table 5. Advantages of new contraceptive methods

Increases range of new contraceptive methods
Very effective and easy to use
Reversible, but not daily hormonal effects with better compliance
Low hormone doses
Continuous low hormone levels

ORAL CONTRACEPTIVES

One of the most popular contraceptive methods is the oral contraceptive pill (OCP) and there are over 145 brands of OCPs available worldwide; most OCPs contain both a synthetic estrogen and synthetic progestogen (see table 6) (l ,2,42). The estrogen is usually ethinyl estradiol (EE), but a

few brands contain mestranol. In general, it is thought that 30-35 mcg EE is equivalent to 50 mcg of mestranol (see table 6). There are many progestogens available, including norethindrone, levonorgestrel, gestodene, desogestrel, norgestimate, ciproterone acetate, and drospirenone. Drospirenone is a newer synthetic progestin chemically related to spironolactone (43). Estrogen may lead to nausea, headache, weight gain, breast tenderness, and breast enlargement; progestins may lead to unfavorable changes in low density lipoprotein (LDL) and high density lipoprotein (HDL) cholesterol, fatigue, depression, and menstrual changes. Questions to pose to the adolescent interested in oral contraceptives are listed in table 7.

Table 6. Combined oral contraceptive hormones

Estrogen	
Ethinyl Estradiol	
Mestranol (3 brands)	
Progestins	
Norgestrel	***Levonorgestrel***
Norethindrone	Norgestimate
Norethindrone acetate	Desogestrel
Ethynodiol acetate	Drospirenone
Gesrodene: (not available in the US)	

Table 7. Questions to pose to teens requesting contraception

1. What methods have you used before?
2. What are your worries about this method?
3. What method do your friends use? What did they say about these methods?
4. Do you think you can use this method correctly?
5. Do you worry about your weight? Are you dieting?
6. Can you deal with unexpected bleeding?
7. Have you beard of some negative comments about OCP use (e.g., weight gain and infertility?)
8. Do you know the minor OCP side effects?
9. Do you have any questions I have not answered?

OCPs prevent pregnancy by inhibiting ovulation, increasing cervical mucus viscosity, causing endometrial atrophy, and changing tubal transport mechanisms (1). Non-contraceptive benefits of the oral contraceptive are listed in table 8 (1,2,4,15,44). Most brands are manufactured as 21 or 28 day packs. The 21 day packs have seven days of placebo pills, so that the adolescent continues to take a pill each day of the cycle. Newer variations include brands which have only two placebo days in each 28 day cycle. Also available is an OCP dial pack dispenser, with each pill numbered and a dial that only turns in one direction. There is no combined oral contraceptive pill brand shown to be more effective than any other brand in preventing pregnancy; thus, any brand the female wishes to take to prevent unwanted pregnancy is acceptable (1,2,45). Some OCPs can be counterfeit and this possibility must be considered if pills are not obtained in pharmacies or other trusted places (46). Along with OCPs, condoms are also recommended to reduce the risk for sexually transmitted diseases (47,48).

Table 8. Non-contraceptive benefits of combined oral contraceptives (1,2,4)

1. Treatment for dysmenorrhea
2. Treatment for dysfunctional uterine bleeding
3. Treatment for premenstrual syndrome
4. Decreased risk for ovarian and endometrial cancer
5. Decreased risk for symptomatic pelvic inflammatory disease
6. Treatment for polycystic ovary syndrome (PCOS)
7. Treatment of acne vulgaris
8. Treaunent for premature ovarian failure
9. Treatment for endometriosis
1O. Treatment of hypothalamic amenorrhea due to eating disorders, exercise, stress
11. Decreased Mittelschmei1z
12. Prevention of ovarian cyst disease
13. Lower incidence of ectopic pregnancy (reduced risk by 90%)
14. Protective for rheumatoid arthritis
15. Possible benefit in prevention/treatment of disorders associated with decreased bone mineral density
16. Possible benefit in the prevention of the development of leiomyomata uteri

Newer OCP brands now available include Alesse and Levlite (both with 20 mcg EE and 0.1 mg levonorgestrel), Apri (with 30 mcg EE and 0.15 mg desogestrel), Desogen (30 mcg EE with 0.15 mg desogestrel), Estrostep (EE increasing from 20-35 mcgs over three weeks with 1 mg norethindone), Kariva (multiphasic with three levels of EE [20,0, 10] and 0.15 mg desogestrel), and Mircette (multiphasic: three weeks of 20 mcgs of EE and 0.15 mg desogestrol, then 2 placebo pills. then 5 days of 10 mcgs of EE alone). The two brands that are FDA-approved for treatment of acne vulgaris are Estrostep and Ortho Tri-Cyclen, Cyclessa is a low-dose tripbasic OCP that contains less estrogen than Tri-Cyclen and other triphasic pills; it contains 25 mcg/day of ethinyl estradiol plus desogestrel [0.1, 0.125, and 0.15 mg/day] in each phase (49).

Yasmin is an oral contraceptive with 30 mcg of EE and the progestin, drospirenone (43). This progestin is a synthetic version of progesterone as well as a spironolactone analog that can lead to potassium retention; 3 mg of drospirenone is equivalent to 25 mg of spironolactone. This OCP is contraindictced in females with renal, hepatic or adrenal insufficiency (43). It is unclear if this OCP has any advantages over other OCPs and its effect on acne is similar to other OCPs. One report notes 40 cases of VTB with 2 deaths in Europe in women taking Yasmin (50).

Seasonale is an OCP with 30 mcg EE and 0.15 mg levonorgestrel (51). It provides continuous combined estrogen plus progestin for 84 days followed by seven days of placebo, so that only four menses occur per year. Lybrel is another continuous use oral contraceptive that contains 0.09 mg of levonorgestrel and 0.02 mg of ethinyl estradiol. This extended cycling (e.g., absence of menses for several months) is especially helpful for adolescents who have medical problems that are worsened by menstruation or have significant adverse symptoms due to menstruation, such as dysmenorrhea or menorrhagia (see table 9) (52). However, extended cycling is associated with increased breakthrough bleeding, especially in the first year of use (51). Some females may be interested in extended cycling for life style reasons. For example, an athlete may wish to extend her cycle to avoid menses during athletic competitions or vacations. Extended cycling can be accomplished with any OCP by omitting the placebo pills and starting a new pack of OCPs

after 21. days. The Patch and NuvaRing have not been studied for extended or continuous use regimens.

Table 9. Conditions that may benefit from extended cycling

Dysmenorrhea
Premenstrual Tension Syndrome (PTS)
Menorrhagia
Iron Deficiency Anemia
Endometriosis
Headaches
Epilepsy
Rheumatoid Arthritis
Coagulapathies
Anticoagulation Therapy

Contraindications to OCPS

The World Health Organization (WHO) has published a list of medical eligibility guidelines to provide clinicians with guidelines for OCP use in those with various chronic illnesses that place users at increased risk of complications (see table 10) (49,53-56). Females in WHO category 1 have no restrictions to use of the OCP, while females in category 2 have some increased medical risk. though pregnancy risks typically exceed OCP risks. Those in category 3 are typically not prescribed an OCP due to increased risks, unless pregnancy risk is high and there is no other method of contraception that is acceptable to the patient. If a condition places the female in category 4, the individual should not be placed on OCPs due to the high risks of significant OCP-induced adverse effects.

Table 10. WHO medical eligibility categories for OCPs)*(56-58)

Category one (no restrictions)
Antibiotics
Benign breast disease

Benign ovarian tumors
Cervical ectropion
Dysmenorrhea,
Endometriosis
Epilepsy
Family history of breast cancer
Gestational trophoblastic disease (benign or malignant)
Headaches (mild)
History of ectopic pregnancy or abortion (postabortion after first or
second trimester),
History of gestational diabetes
Increased STD risk
Iron deficiency anemia
Irregular menstrual bleeding
Obesity
Ovarian or endometrial cancer
Past pelvic surgery
Pelvic inflammatory disease
Postpartum at or over 21 days
Thyroid disorders (as hypo/hyperthyroidisrn, simple goiter)
Varicose veins
Various infections :malaria, tuberculosis, others)
Sexually transmitted diseases
Viral hepatitis carrier

Category two (caution)

Cervical cancer
Diabetes mellitus (uncomplicated)
Headaches (severe and if they start after beginning OCPs)
Hypertension at 140-159/100-109 mm Hg
Major surgery without prolonged immobilization
Migraine headaches without focal neurologic involvement,
Patients who have a hard time taking the OCP correctly:
drug or alcohol abuse
mental retardation
persistent history as poor OCP takers
severe psychiatric disorders
Sickle cell disease or sickle C disease

Undiagnosed breast mass

Category three (usually OCP not given unless risks for pregnancy are higher than the OCP)

Gallbladder disease
Lactating (6 weeks to 6 months),
Less than 21 days postpartum
Medications that interfere with OCP efficacy
Undiagnosed abnormal vaginal/uterine bleeding.

Category Four (OCP contraindicated)

Breast cancer
Cerebrovascular accident (active or history)
Complicated structural heart disease (with pulmonary hypertension, atrial
fibrillation of history of subacute bacterial endocarditis)
Coronary (or ischemic) heart disease (active or history)
Deep vein thrombosis or pulmonary embolism (active of history)
Diabetes mellitus (complicated with retinopathy, neuropathy, nephropathy)
Headaches (including migraine headaches) with focal neurologic symptoms
Hypertension (severe: (160+/110+ mm Hg or with vascular complications)
Lactation under 6 weeks postpartum
Liver disease (including liver cancer, benign hepatic adenoma, active viral
hepatitis, severe cirrhosis)
Pregnancy, complicated
Surgery (involving the lower extremities and/or prolonged immobilization

*(World Health Organization, 1996, 2000; Pettinato, 2003)

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CARDIOVASCULAR RISKS AND OCPs

Research has indicated an increased risk of cardiovascular complications in females on OCPs (50,57-68). Obese and non-obese females on birth control pills have an increased risk for pulmonary emboli, thrombophlebitis, and vascular thromboses. Some studies note a greater incidence of myocardial infarction and subarachnoid hemorrhage as well (50). An absolute OCP contraindication is a past history of venous thrombosis (VT) and the risk of VT is more significant for the adolescent or young adult than arterial thrombosis. Significant obesity is a VT risk factor and the risk is increased in obese OCP users (58-60). Table 11 notes risk factors for thrombosis. In 2008 the US Food and Drug Administration (FDA) added a label to the birth control patch that patch users were at higher risk for venous thromboembolism than OCP users, since patch users are exposed to higher estrogen levels than noted with OCP users.

Table 11. Causes of thromboses

Factor V Leiden mutation
Prothrombin mutation G20210A
Protein S Deficiency
Protein C Deficie1tcy
Antthrombin III deficiency
Hyperhomocysteinemia from mutations in MTHFR gene
Deficiencies of Proteins: C, S, and antithrombin III
Tobacco use
Other medical risk factors: immobilization, surgery, severe illness
Others: cancer or pregnancy

Cardiovascular deaths from venous and arterial complications in non-smoking females aged 20-24 years is 2-6 per million per year (57). There is a 3-6 fold increased lisle factor for VT development in OCP users and the risk for VT is higher with desogestrel versus levonorgestrel (15,57, 61). The VT risk in the general population is 4 per 100,000 women per year, 10-30 for those on OCPs, and 60 for females who are pregnant or postpartum (57,62-64) (see table 12). Most individuals who

develop venous thrombosis do not have identified VT risk factors (see table 11).

Table 12. Rate of non-fatal tbromboembolism in females (57,62-64)

1. No risk conditions: 4/100,000
2. Low-dose OCPS: 10-30/100,000
a. 10-15: on norgestimate or levonorgestrel OCP
b. 20-30 on desogestrel OCP
3. Pregnancy: 60/100,000
4. Factor V Leiden mutation: 140 if on the OCP (32 if not on the OCP)

Table 13 lists screening questions to use when considering OCPs for contraception. In general, if there is no overt positive family history for VT in those under 50 years of age, one does not need to screen for factor V Leiden or other prothrombotic mutations because of lack of cost-effectiveness. However, the Factor V Leiden mutation is the most common genetic cause of thrombophilia, with a prevalence of 3.6% in asymptomatic women, and 23% among Caucasian women with first episode of spontaneous venous thromboembolism. Factor V Leiden accounts for up to 20% of first-time VT-this prothrombin mutation leads to a 2-4 times increased risk for VT. Thus, the OCP and the patch should not be used if there is a history of thromboembolism. The mini-pill (progestin-only) can be used in this situation. Other contraceptives that can also be used include Dcpo-Provera, Mirena IUD, and barrier methods.

Table 13. Questions about personal/family history of thromboembolism

1. Have you or a close family member (FM) (including uncles/aunts) have blood clots in legs or lungs?
2. Have you/close. FM been hosp. for blood clots in legs/lungs?
3. Have you or FM taken blood thinner?
4. Under what circumstances did the clot form:
Cancer Airline travel Pregnancy
Obesity Immobility Others

Congenital heart disease

The concern with, using OCPs in those with congenital heart disease is that complications may arise because of increased risk for thromboembolism (TE) and endocarditis. Increased risk for TE is due to increased circulation of clotting factors from estrogen because of stimulation of serum globulins from the liver. OCPs and the patch are contraindicated in cardiac conditions with cardiac shunts, congestive heart failure, low output cardiac disorders, and coronary heart disease (62,65-68). The OCP and patch should be avoided in those with cyanotic heart disease and pulmonary hypertension.

Progestin-only contraceptive methods are acceptable for most females with congenital heart diseases including the mini-pill and Depo-Provera (DMPA) if the patient is stable; these patients typically are on anticoagulation as well. The Mirena intrauterine device (IUD) and barrier contraception are safe as well in these situations. Patients with valvular heart disease and congenital heart disease are at risk for endocarditis for one month or so with and after an IUD placement. Other IUD complications at the time of IUD placement include bradycardia, seizures, and syncope; the IUD is contraindicated if the female is on anticoagulation, since there is increased risk of bleeding with the IUD placement. These contraceptive methods are reviewed later in this discussion.

Hypertension

There is a small increase in blood pressure on the OCP with a 6-8 mm Hg rise in the systolic pressure and a 4-6 mm Hg is the diastolic pressure. Blood pressure should be monitored on the OCP and a low-dose OCP is acceptable for stable hypertension with no end organ disease (67). OCPs are contraindicated in those with severe hypertension (i.e., systolic blood pressure > 160 mm Hg and/or diastolic blood pressure >100 mm Hg) (67). The risk of ischemic complications is probably slightly increased in patients with hypertension on OCPs; the US studies suggest no risk, while European studies note some increased risk (65-68).

Other contraceptives that are safe for patients with hypertension are Depo-Provera, the Mirena IUD, and barrier methods.

Hyperlipidemia

Estrogen can worsen lipid patterns (increase low density lipoproteins [LDL] and decrease high density lipoproteins) to increase risks for coronary artery disease (CAD) risks; estrogen can also increase triglycerides, but not to worsen CAD risks (66). Low-dose OCPs are safe for stable hyperlipidemia but should be avoided when the LDL is over 160 mg/dl, triglycerides are over 250 mg/dl, or when multiple CAD risk factors are present (65,66,68). These CAD risk factors include smoking, obesity, diabetes mellitus, hypertension, and positive family history for premature CAD (1,2,4). Progestin-only contraception are safe with hyperlipdemia.

Obesity

Sexually active obese teens who do not want to become pregnant also need contraception. Research notes that overweight/obese youth use contraception less than their normal weight peers and obese females have reduced efficacy with OCPs as well as the patch because of higher adipose tissue sequestration, increased enzyme metabolism in the liver, and higher basal metabolic rates (60,69). However, OCP efficacy in obese females is higher than that noted with the use of barrier contraception. OCPs can be a good contraceptive option for females with obesity, polycystic ovary syndrome, acne, and hirsutism (44). In addition, adverse pregnancy outcomes in Ibis group must be taken under consideration (58,59, 70-72). VT risks are increased in obese females and progestin-only contraception (i.e., the mini-pill and Depo-Provera) can be safely used. However, there can be increased weight gain and central redistribution of adipose tissue following use of Depo-Provera. Also effective in obese individuals are the intravaginal ring and the IUD. In conclusion, the safest methods of contraception for obese female adults may be the mini-pill and the levonorgestrel IUD (58).

Diabetes mellitus

Research notes that OCPs are safe and effective in females with well-controlled diabetes mellitus (types 1 and 2) who do not have such diabetic complications as retinopathy, nephropathy, or peripheral vascular disease (58,60). Metabolic status in diabetes is not worsened on OCPs or the patch and the newer progestins (i.e., desogestrel, norgestimate, or gestodene) may effect metabolism of carbohydrates less than older progestins (66). OCPs should not be provided if there is a history of VT, diabetic complications, or hypertension (58.60). Other safe methods of contraception for diabetic youth include the IUD and the mini-pill (59). If an IUD is placed in a diabetic youth, there may be an increase in recurrent vaginal yeast infections that are resistant to standard anti-fungal management. Depo-Provera is safe and effective in those with diabetes, including when diabetic complications are present (65,66).

Thyroid disease

All contraception should be safe and effective in those with hyper- or hypothyroidism; however, if the youlh is on levothyroxine for hypothyroidism, check T_4 and TSH levels after two cycles of OCPs (65,66).

Hyperprolactinemia

If pituitary adenoma is not the cause, OCPs are safe and also helpful to prevent further bone loss and provide effective concraception (65).

Migraine headaches

Migraine association with menses (catamenial headaches) may be due to reduced estrogen levels at menses (65). OCPs are not contraindicated in tension or muscular-type headaches, though the OCP should be stopped if the female presents with severe, worsening headaches after slatting the

OCP. Caution is recommended in using OCPs in females with a histo1y of migraine headaches. OCPs should be stopped or avoided in those with migraines that worsen on OCPs or in those with migraines complicated by neurological features (i.e., auras) (1,2).

Those with migraines and neurological symptoms (i.e., complicated migraines) have an increase risk for cerebral ischemia and cerebrovascular accidents (CVAs) on the OCP because of the estrogen component (73). Studies in Europe noted a four fold increase in ischemic strokes in females with complicated migraines on the OCP while studies in the United States suggest a two-fold increase (66). The risk of thrombotic stroke in migrainoid females on OCPs is 8 per 100,000 at age 20 years versus 80 at age 40 years of age (66).

In summary, OCPs should not be given to those with severe migraines or complicated migraines, including those with hemiplegic or ophthalmoplegic types. Stop the pill if the headaches worsen in OCPs. Those with focal neurologic features (i.e., hemiplegic or ophthalmoplegic types) are given a WHO category of 4 (contraindication), because of the high risk for CVAs on OCPs. If headaches without focal neurologic features start after the OCP has begun, a WHO category of 2 is given. If complex migraines are present, avoid estrogen and consider Depo-Provera, the mini-pill, or the Mirena IUD in addition to barrier contraceptives (58,59).

Epilepsy

One million females of child-bearing age have a seizure disorder and may have reduced efficacy if placed on certain anti-epileptic medications (74-77). Catamenial epilepsy may occur because of hormonal changes that occur during the menstrual cycle (77). Estrogen has proconvulsant effects and progestin has anti-convulsaut effects (74-76). Puberty itself does not usually worsen or improve epilepsy of childhood, though juvenile myoclonic epilepsy may develop as puberty ensues (77). However, if seizure activity does worsen with puberty, an adjustment in anti-seizure medications usually corrects the situation. Ethinyl estradiol undergoes considerable first-pass metabolism as noted in table 14 while the metabolism of progestins in summarized in table 15.

Table 14. Metabolism of ethinyl estradiol

1. In the Gastrointestinal tract by sulfation
2. In the liver by glucuronidation or hydroxylation
a. Enzyme CYP3A4 is 1 of 7 primary isoenzymes of the P-450 enzyme system
b. CYP3A4 catalyzes the hydroxylation
3. Metabolites under conjugation and enterohepatic recirculation (results in reabsorption of active EE)
4. Extent of enzyme induction varies depending on genetic+ environmental factors

Table 15. Metabolism of progestin

1. Synthetic progestins are eliminated through hepatic metabolism.
2. Progestins do not undergo extensive first-pass metabolism or enterohepatic recirculation
3. CYP3A4 isozyme is involved in progestin metabolism
4. Inducer anti-epileptic medications ↑ sex hormone-binding globulins that ↓ P
5. Levels

However, many antiepileptic dmgs (AEDs) can induce an increase in hepatic microsomal enzymes (cytochrome P-450 system), which can produce increased pill metabolism and decreased pill hormone concentrations. The result is a decrease in the pill's contraceptive ability (increased estrogen [E] metabolism, increased progestin [P] protein binding, decreased E & P concentration with decreased contraceptive efficacy) (76), resulting in an estimated 3.1 pregnancies per 100 women years of use; this pregnancy rate can be significant when considering the potential teratogenic effects of AEOs on the developing embryo (74-76). Hepatic enzyme inducer anti-epileptic drugs are listed in table 16.

Table 16. Inducer anti-convulsant medicatations (1,57,63,72, 74)

Phenytoin (Dilantin)
Phenobarbital
Primidone (Mysoline)
Felbamate (mild inducer) (Felbato)
Carbamazepine (Tegretol)
Oxycarbazepine (mild inducer) (Trilepal)
Topiramate (mild inducer) (Topamax)
Tiagabine

Newer AEDs have minimal interaction with OCPs. Table 17 lists anti-epileptic drugs (AEDs) that do not cause such interference because they do not inhibit hepatic microsomal enzymes; they include valproic acid (Depakote) and zonisamide (weak inhibitor [Zonegran]) and those with no effect on P-450 enzymes and no decrease in estrogen or progestin levels. Use of OCPs and lamotrigine may reduce lamotrigine levels and close monitoring is recommended (74-76). There can also be drug interference in those taking AEDs, OCPs., and other drugs that are metabolized via the P-450 pathway, that affect drug concentrations; these include ketoconazole, fluoxetine, erythromycin, propoxyphene, others. AEDs have various side effects including increased sexual dysfunction, irregular menses, and ovulatory failure. For example, valproate has increased risks for anovulation, polycystic ovarian syndrome, polycystic-appearing ovaries, and hyperinsulinemia.

Table 17. AEDs that do not effect OCP hormonal levels (1,57,63,72, 74)

Gabapentin (Neurontin)
Ethosuximide (Z rontin)
Tiagabine
Lamotrigine(Lamietal)
Levetiracetam (Keppra)
Pregabalin
Vigabacrin (Sabril)

Management: Epilepsy and OCPs

Some clinicians conclude that the contraceptive efficacy of inducer AEDs with OCPs is acceptable and use these AEDs along with the OCP. Some clinicians seek to avoid such interference by prescribing higher estrogen OCPs (i.e, 50 mcg to 100 mcg ethinyl estradiol) when patients are taking inducer AEDs, while other clinicians increase the frequency of OCP closing and reduce the pill-free interval of seven days along with adding barrier contraception (74-76). A more potent progestin may be used if break-through bleeding occurs. As noted, anti-epileptic drugs do have a teratogenic potential and thus, these patients should take folate to lower the risk for neural tube defects, while also taking calcium and vitamin D supplementation to lower risks for AED-induced bone disease (78).

The amount of AEDs can be altered during the menstrual cycle to reduce side effects. For example, chose with reduction of the AED during the OCP placebo week may experience reduced drug-induced headaches (66). The mini-pill has reduced contraceptive efficacy in those on AEDs, due to low progestin levels and is not recommended. However, Depo-Provera is effective and may have anti-convulsant effects, though it has not been studied in this regard. The IUD (Mirena and copper) and barrier contraception are also recommended in patients on inducer AEDs that need contraception.

Arteriovenous malformation (AVM) with epilepsy

There is no increase in a hemorrhagic complication in those with an AVM and epilepsy during pregnancy or labor, if the AVM has been surgically treated. There is no research that the OCP will increase thrombosis in a patient with an AVM on an OCP (79). An AVM in the gastrointestinal tract may have reduced bleeding risks on OCPs (79).

Liver disorders

Estrogen and nor-progestins are metabolized in the liver and alter hepatocellular function, leading to increase in cholesterol, reduction in

bile acid as well as bile secretion, and changes in bile composition. OCPs should not be provided for those with active liver disease (WHO category 4), including cirrhosis and hepatitis (65).The OCP or patch can be used if liver function returns to normal, though the effect of obesity-related NASH (nonalcoholic steatohcpatitis) on OCPs is not clear at this lime. Depo-Provera is acceptable unless there is increased risk for bleeding, while barrier contraception and the Mirena IUD are acceptable contraceptive methods if active liver disorders are present. The birth control pill-associated hepatic cell adenoma has an estimated annual incidence of 3.4 cases per 100,000 pill users. A variant of this benign tumor is the focal nodular hyperplasia; on rare occasions this lesion can rupture in the liver or peritoneum, causing a syndrome of right upper quadrant mass, abdominal pain, right shoulder pain, and diverse symptomatology associated with acute blood loss (1,2).

Renal disease

Pregnancy can worsen renal prognosis in those with end-stage renal disease (ESRD) who are not on dialysis and those who are post-transplant. OCPs are safe and effective for females with ESRD, if the renal condition is stable and there is no unpaired renal function, hypertension, cardiovascular disease, or thromboembolism (65,66). Systemic lupus erythematosus is considered below. In those with stable renal disease, acceptable contraceptive methods include OCPs, the patch, Depo-Provera, the Mirena IUD, and barrier contraceptives. OCPs are useful for stable renal disease without complications and are beneficial to control the hype1menorrbea often seen with chronic renal disease. Estrogen should be avoided in those with chronic renal disease who have significant hypertension or are bed-ridden; alternative contraceptives in such situations include progestin-only methods or the Mirena IUD. The IUD should be avoided in those with risk of infections (i.e., endometritis) and with worsening anemia.

There is limited research at this point to guide decisions regarding contraception for sexually active renal transplant females. The medications that the renal transplant patient takes should be considered, as well as the specific complications when advising on specific

contraceptive methods (80). Those on estrogen contraceptive methods should be carefully monitored, while Depo-Provera and banier methods seem to be safe. Use of IUDs may cause complications, since these females are on immunosuppressive medications and are imo1uoocompromised because of their chronic renal disease. IUDs should be avoided in those on peritoneal dialysis because of the risk of peritonitis with run insertion; if the IUD is inserted, prophylactic antibiotics should be prescribed (80,81).

Pulmonary disorders

Some adolescent females with cystic fibrosis are fertile and are at risk for pregnancy if sexually active. Thus, contraception is appropriate to discuss with sexually active females who have cystic fibrosis. The concern is that the progestin in OCPs may thicken bronchial mucus as it does cervical mucus. However. interference with contraceptive efficacy has not been observed and progestin is not contraindicated in those with cystic fibrosis (82). Pulmonary embolism is a rare complication of OCPs, as noted before. The Mirena IUD and barrier contraceptives are safe for those with cystic fibrosis (65). Also, there is no OCP contraindication for females with asthma. Patients with tuberculosis who are placed on anti-tuberculosis therapy, such as rifampin, will have reduced OCP effectiveness.

Inflammatory bowel disease

Menstruation can worsen inflammatory bowel disease (IBD) symptoms because of menstrual-induced rise in prostaglandin levels that can worsen contractions of the uterine and gastrointestinal muscles. Pregnancy is not very common in females with inflammato1y bowel disease (IBD), and can worsen the IBD condition. OCPs can reduce gastrointestinal symptoms in IBD if taken with active colitis; however, there can be limited OCP absorption with less pill effectiveness and increased break-through bleeding in this situation. However, contraception should be provided to sexually active females with IBD (83). Thus, the patch may

be best to avoid the need for gastrointestinal absorption. Depo-Provera is effective and can be useful to reduce the incidence of menstrua1 bleeding and subsequent anemia. Depo-Provera may be recommended in the small percent of cases in which there is concomitant IBD and a coagulation disorder. Bone density issues should be taken under consideration, especially if corticosteroid therapy is administered. Barrier contraceptive methods are safe for those with IBO who need contraception. The Mirena IUD should be safe though research is needed to further su1dy its use in those with IBD.

Cancer

OCPs are absolutely contraindicated in females with breast cancer, though they may reduce the risk for ovarian and endometrial carcinoma (1,2,84). However, estrogen and progestin receptors are found in ovarian cancer tissue and OCPs arc avoided with ovarian cancer.

Cancer treatment: Chemotherapy and radiotherapy

If thrombocytopenia (TCP) is present, OCPs are effective and beneficial to stop TCP-induced bleeding. Continuous OCP use is helpful, while cyclic OCPs should be avoided for severe or prolonged TCP. OCP absorption is reduced if there is emesis or mucositis. OCPs should be avoided if severe gastrointestinal side effects develop.. For example, the gastrointestinal flora may change as a result of treatment-induced diarrheal cycles. The presence of infections or antibiotic use alter gastro-hepatic circulation that can result in reduced OCP effectiveness. The OCP should be avoided in those with a history of thrombosis, as noted earlier.

Drug interactions may affect OCP use, as for example, with rifampin or rifabutin that can decrease OCP levels. Also, OCPs can reduce drug clearance, as, for example, noted with prednisolone. Careful monitoring is needed if cyclosporine is used, while OCPs should be avoided in those receiving allogenic bone marrow transplants taking cyclosporine and prednisolone in order to prevent the development of graft-versus-host disease and graft rejection.

Other contraceptives in cancer patients

The mini-pill is the first choice of contraception if the patient is receiving chemotherapy; ii should be avoided with a positive history of an ectopic pregnancy and if the patient is taking certain medications such as griscofulvin, rifampicin, or some anti-convulsant drugs. If there is active vomiting or mucositis, OCP absorption may not occur. Depo-Provera is not given if chemotherapy occurs due to the potential occurrence of infection with blood cell changes (i.e., neutropenia or thrombocytopenia [TCP]) or the occurrence of hematoma with an injection. Depo-Provera may worsen bone loss already noted in some receiving chemotherapy. Contraceptive implants can cause complications in those with TCP and irregular bleeding, while these potential difficulties can be acceptable if the patient is stable and only brief or transient TCP occurs. The IUD should be avoided in females with neutropenia and a TCP.

HIV

Drug interactions may occur between HIV medications and OCPs. For example, some HIV medications (as efavirenz or atazanavir) increase ethinyl estradiol, while others (nevirapine and lopinavir/ritonavir) decrease estrogen (59,85). Depo-Provera is effective in females with HIV and there is minimal interaction with HIV medications, such as nelfinavir, efavirenz, nevirapine or nucleoside analogues (85,86). The IUD is also effective and safe in patients with HIV.

Rheumatological disorders (RD)

The use of OCPs is problematic in females with rheurnacologic disorders (RD) because of the concern with the risk of thrombosis and potential RD exacerbations. These risks are worsened with the amount of ethinyl estradiol and progestin type (87). Research suggests that there is no worsening of systemic lupus erythematosus (SLE) or increased SLE flare ups if these females are taking OCPs and the patient has stable SLE (87). There may be drug interactions between RD medications and OCPs. Estrogen-containing contraceptives should be avoided in those with

antiphospholipid antibody (aPL) syndrome because of an increased risk for thrombosis, as noted below. Progestin-only contraception should be used in those with aPL syndrome if a reduction in menstrual bleeding is needed (as with Depo-Provera) and if the patient needs anticoagulation.

Antiphospholipid-antibody (aPL) syndrome

Thrombosis is increased in aPL syndrome, especially if there are additional risk factors, as noted in table 11. The SELENA study (Safety of Estrogen in Lupus Erythematosus National Assessment) concludes that OCPs should be avoided in patients with aPL syndrome who have moderate or high titers of antiphospholipid antibodies (i.e., at or over 40 GPL or MPL units); progestin-ooly contraception should be used and Depo-Provera is an acceptable contraceptive agent (87). The Mirena IUD is also acceptable for those with the aPL syndrome.

SLE (systemic lupus erythematosus)

There is no increase in SLE exacerbations in females with stable SLE who ate placed on OCPs and thus, OCPs are used for contraception in these females (66,87,88). Patients with SLE should be screened for aPL syndrome and the estrogen avoided if there is aPL syndrome, vasculitis, or nephritis (88). More research is needed regarding use of the OCP patch, but increased hormone levels are noted and thus, the patch should be avoided if the OCP is contraindicated. Drospirenone (as noted in Yasmin) can lead to hyperkalemia and is avoided in renal insufficiency. The mini-pill and barrier contraception are acceptable for those with SLE, while Depo-Provera is avoided because of bone loss issues associated with this contraceptive. An IUD may lead to increased risk for infection in SLE patients because of decreased immunity, though more research is needed in this regard.

Rheumatoid arthritis (RA)

OCPs and the contraceptive patch have not been shown by most research to increase RA exacerbations, but neither do they do improve RA (87). Androgenic OCPs with second generation pills might be best to maximize androgenic immunosuppression. Females with severe RA might have problems with insertion of diaphragms or vaginal rings. Though research is limited, it is best to avoid IUDs for females with RA who are taking immunosuppressivc medications, because of potential infection risk. The use of barrier contraception or the TUD may also be physically difficult in some RA patients.

The use of OCPs has not been shown to increase exacerbations of Raynaud's disease. However, OCPs shot d be avoided if there is risk of ischemia, atherosclerosis, or vasc11litis. There may be d111g interactions between OCPs and RA drugs, such as corticosteroids, warfarin, cyclosporin, and certain anticonvulsants. OCPs. the patch, and the vaginal ring should be avoided in RA females with prolonged immobilization and the OCP should be stopped before surgery; the timing is varied and ranges from two weeks to two months before planned surgery, due to negative effects of estrogen on coagulation. Some clinicians perioperatively add heparin in such cases, in order to reduce the risk for venous thrombosis (VT), particularly if there are other VT risk factors present. Others add a progestin-only contraceptive method when estrogen is stopped. Some clinicians have used Depo-Provera once before surgery if contraception is needed .

Sickle cell disorders (SCD)

Pregnancy increases risks for both the mother with SCD and fetus and thus, contraception is important for sexually active females with SCD who do not wish to become pregnant. Since the phenomenon of sickling in SCD is not a process of thrombosis, there is no known increased thrombosis risk in females with SCD in OCPs; thus, OCPs should be safe for these females, though research is limited in this regard. In addition to effective contraception. limited research suggests that Depo-Provera may reduce sickling in SCD and may be the best method of

contraception for females with SCD [1,65]. Barrier contraceptives are also safe in females with SCD.

Intellectual disability (mental retardation)

OCPs, the patch, and ba1Tier contraception may be difficult to use because of limited cognitive skills in sexually active females with intellectual disability (16,65,66). The most popular method is Depo-Provera, though the issue of osteopenia should be monitored in these female adolescents. The intrauterine device bas been used as well (89,90). Sterilization remains a controversial issue in adolescent females with mental retardation.

Schizophrenia

It is difficult for females with schizophrenia to take OCPs daily or use the patch effectively; worsened moodiness may occur on some taking oral contraception. The IUD may become a delusional focus for some schizophrenic females and it can be very difficult to recognize JUD. induced infection when the patient is delusional (91}. The best contraceptive method for sexually active females with schizophrenia may be Depo-Provera.

Drug interactions

Clinicians should review any other medications patients on OCPs are taking. in order to consider possible drug interactions (see table 18) (74,92). For example, antacids (aluminum and magnesium types) prevent gastrointestinal absorption of OCPs, especially the progestin component; thus, ingestion of OCPs and antacids should be separated by at least three hours. Broad spectrum antibiotics do not interfere with OCPs, though previous anecdotal reports suggested the opposite (1,2). However, interference is noted with some drugs, such as rifampin, griseofulvin, ketoconazole, and itraconazole. Serum levels of some medications can be

affected if the patient is on OCPs, such as tricyclic antidepressants, cyclosporine, caffeine, theophylline, and prednisolone. Warfarin levels may be increased or decreased, while free thyroxine levels are reduced on OCPs due to increased levels of thyroxine binding globulin.

Table 18. Potential drugs interactions with OCPs (92)

I. Potent hepatic enzyme inducer with decreased contraceptive efficacy
- a. Rifampin
- b. Griseofulvin
- c. Ketoconazole; itraconazole

II. Hepatic enzyme inducer w/o evidence of reduced efficacy
- a. Phenobarbital
- b. Phenytoin
- c. Carbamazepine
- d. Primidone
- e. Elhosuximide

III. Meds that reduce EE levels with increased breakthrough bleeding (BTB); no decreased efficacy
- a. Tricyclic antidepressants
- b. Chlordiazepoxide; diazepam
- c. Theophylline

4. Other Reported Drug Interactions with COCs*
- a. Aspirin; acetaminophen
  - 1) Increased clearance of these meds if COCs added
  - 2) Anedotal (not proven) rec: increase med doses
- b. St. John's wort
  - 1) Inhibitor of P450 isoenzymes
  - 2) Increased breakthrough bleeding
  - 3) Anecdotal evidence of reduced OC efficacy

*Glasier A: Drug interactions and combination oral contraceptives. Dialogues in Contraception (Univ. So. CA) 6(5): 1-4, 2000 (http://dialogues.usc.edu)

Miscellaneous

As previously noted, a number of minor side effects may occur with OCP use including nausea, headaches, mood changes, and breast tenderness; these adverse effects can be quite troublesome to adolescent females (1 ,2, 31). These often disappear with increasing duration of OCP use. Although many women feel that OCPs are associated with weight gain, there is no convincing evidence that OCPs cause an increase in weight (1,2). Breakthrough bleeding (BTB) is a common side effect of OCP use and one of the most frequent reasons for OCP discontinuation. In most patients, BTB decreases with consistent continued use, and there is no need to change OCP brands because of this side effect. However, if BTB is severe and/or unrelenting, switching to an OCP containing norgestrel (e.g., Lo/Ovral®), norgestimate (e.g., Ortho-Cyclen®) or levonorgestrel (e.g., Nordette®, Triphasil®) may be helpful. One can also recommend taking two pills a day until the bleeding stops or adding 20 mcg of ethinyl estradiol for 7-10 days. It is rare that a pill with 50 mcg of ethinyl estradiol is needed to control such bleeding.

TRANSDERMAL HORMONAL CONTRACEPTION

Use of transdermal mechanisms for delivery of medication became available in the early 1980s. Medications that are now available in transdermal formulations include clonidine, estradiol, fentanyl, nicotine, nitroglycerin, scopolamine, and testosterone (93-95). The FDA approved the first transdermal contraceptive patch (Ortho Evra Patch) in November of 2001. It has similar side effects as OCPs with the addition of mild to moderate application site reactions and increased incidence of breast symptoms and dysmenorrhea (95-101). It is not yet clear if the patch offers any significant increase in efficacy or safety advantages over OCPs (95). However, this method may improve compliance in some women.

The contraceptive patch is a matchbook size device placed on the skin (abdomen, upper outer arm, buttocks, upper torso [not the breasts]). It consists of a three-layer matrix with an outer polyester protective layer (light tan in color), a middle layer that contains adhesive as well as

contraceptive steroids, and an inner, clear polyester liner that is removed before skin application (96,97). The patch results in a daily hormone release of 20 mcg ethinyl estradiol and 150 mcg of norelgestromin, the primary active metabolite of norgestimate (94,98-104). The hormones are rapidly absorbed into the blood and a steady state is reached in two days, similar to that noted with the oral contraceptive Ortho-Cyclen. The patch is started on day l of menses, replaced weekly for three weeks, and week four is patch free. Each patch should be placed at a different site.

Using the contraceptive patch does not require direct genital contact or daily compliance that makes this contraceptive method popular with many adolescent females (105). Some may find that using the patch is more convenient than daily pill dosing as well as more user controlled and more readily reversible than Depo-Provera. ln addition, for those who have difficulty swallowing pills or gastrointestinal disturbances with OCPs, the patch may be a good alternative. There are no hormonal peaks and troughs as noted with OCPs, and cycle control as well as ovulation suppression is similar to Ortho-Cyclen (98-106).

As noted, the adverse effects of the patch include potential site reactions (l.9%), a transient increase in breast tenderness, and also an increase in dysmenorrhea (94,103,107,108). Breast symptoms may increase with use of the patch and severity ranges from mild to moderate. Cardiovascular side effects may be increased due to increased hormone levels (109,110). Obesity (i.e., weight > 90 kg) results in reduced contraceptive efficacy, but still higher than tbat noted with barrier contraceptives (58,59,98). Dermatitis may occur with the patch and those with exfoliative skin diseases or history of skin allergies may not be appropriate for the patch. Break-through bleeding and/or spotting may be more prevalent in menstrual cycles 1 and 2, than noted with OCPs. The incidence of nausea, emotional lability, and headaches are similar to that noted with OCPs. The patch produces a similar lipid profile, as noted with other OCPs containing EE and norgestimate (111).

Pregnancy rates in adult women are similar when comparing the OCP and the patch, with pregnancy rates of 0.7 -1.24 per 100 women-years reported with the patch versus 2.18 for OCPs (98-104). Adequate steroid levels are maintained for two days past the manufacturer's recommended 7-day application. The efficacy is similar with various application sites. This rate is not affected by warm humid climates,

vigorous exercise or exposure to saunas or water baths. Table 19 notes reasons for contraceptive failure with patch technology.

Table 19. Causes of contraceptive failure with patch technology

1. Keeping the patch on for over 7 days
2. Detachment of the patch
3. Failure to begin a new patch after 7 days being off the patch

Of the 15 pregnancies reported during clinical trials of the patch. 5 were in women who weighed over 90 kg (198 pounds) (2,62). This finding led to a warning from the manufacturer that the patch may not be as effective in obese women. However, there has been little research on the efficacy of other hormonal contraceptives in obese females, so this finding may not be limited to the patch. Of over 70,000 patches that were used in adult females during clinical trials, only 4.7% were replaced because they fell off (1.8%) or were partially detached (2.9%) (62). However, one study of adolescents ages 15 to 18 noted a complete or partial detachment rate of 35.5% (62). If the patch is off after 24 hours, there is a need for back-up contraception for the next 7 days.

PROGESTIN-ONLY PILLS (POPS; MINI·PILLS)

Contraceptive mechanisms of progestin-only pills (POPs) include thickening of the cervical mucus and endometrial involution. Ovulation is not reliably inhibited and pregnancy rates can be 1 to 3 pregnancies per 100,000 (1,2,4,112-114). Progestins used in POPs include 0.35 mg of norethindrone (Micronor; Nor-Q.D) and 0.075 mg of norgestrel (Ovrette). POPs are recommended by some clinicians when estrogen is contraindicated (e.g., patients who have severe hypertension or coronary heart disease). POPs are generally safe for most cardiovascular disorders including cyanosis and atrial or ventricular arrhythmias. Common side effects of POPs include irregular uterine bleeding and amenorrhea; because of the irregular bleeding that POPs can induce, the mini-pill should be avoided in those with coagulation disorders (1,2,4,31).

POPs should not be used by females who have a history of ectopic pregnancy and taking medications such as anticonvulsants, griseofulvin, and rifampin. POPs are not contraindicated in females with obesity; there is no increase in VT in obese females on progestin-only pills (58-60). POPs should be avoided if the adolescent has a history of an ectopic pregnancy and irregular menses, if she is clearly a candidate for methods with increased efficacy over mini-pills and if she is unlikely to be compliant with pills. A barrier method (e.g., condoms with diaphragm or with vaginal contraceptives) can be added to improve the overall contraceptive efficacy of the mini-pill.

EMERGENCY CONTRACEPTIVES (ECs)

Emergency contraceptives (Post-coital contraception) are among the most controversial and under prescribed contraceptive methods (see table 20)(115-121). A number of mechanism are noted in pregnancy prevention including delay of ovum maturation, interference with corpus luteum function, thickening of cervical mucus, and others; thus, EC methods interfere with ovulation or implantation (if the egg is fertilized)(119,122). Whenever adolescents seek EC, they should be counseled regarding effective contraceptive methods. A variety of OCPs can be taken after coital activity to prevent pregnancy, including Ovral (two pills followed in 12 hours by two more pills) and various brands which require four pills followed by four pills in 12 hours: Lo-Ovral, Levien and Nordette. In 1998, the FDA approved of the Preven Emergency Kit as an EC, based on the EC method described by Albert Yuzpe in 1974 using two pills (with ethinyl estradiol and levonorgestrel) followed in 12 hours by two more pills.

In 1999. the FDA approved of Plan B, a progestin-only EC method that consists of two tables of 0.75 mg of levonorgestrel (Levonelle). The first tablet of Plan B is taken immediately after unprotected coitus and the second tablet is taken 12 hours later; studies have shown that Plan B is equally effective when both pills are taken at the same time, as soon as possible after coitus (115). Because Plan B contains no estrogen, nausea and vomiting is uncommon and there is no need to obtain a pregnancy test before administration. Thus, Plan B may be better tolerated than

other ECs that contain estrogen (115). Although initially approved for use within three days of coitus, more recent studies have shown that Plan B may be effective in pregnancy prevention if taken up to five days after unprotected coitus (115-120). The expected pregnancy rate of 8% from an episode of unprotected coitus in the second or third week of the menstrual cycle is reduced to < 1 % with Plan B use (115-120). If ECs were more widely available, they could prevent 1.7 million unintended pregnancies and reduce abortions by 50% (116,120).

Table 20. Emergency contraceptives

- Ovral®: 2 tablets followed by 2 tablets in 12 hours
- Lo/Ovral®, Nordette® or Levlen®: 4 labs and 4 more in 12 hours
- TriPhasil® or Tri-Levlen® (yellow tabs only): 4 tabs, and 4 more in 12 hours
- Ovrette®: 20 tabs and 20 more in 12 hours
- Preven® Emergency Contraceptive Kit
- Plan B®: Levonorgestrel: 0.75 mg followed by 0.75 mg in 12 hours

EC is very effective in preventing pregnancy, yet is not well-known among adolescents and college students. Adolescents should be clearly taught that emergency contraceptives can be used in various situations, as listed in table 21 (118,123). Without proper instructions, youth do not use ECs effectively. Providing the emergency contraceptive for the patient to take home before it is needed may improve efficacy (119). Table 22 lists barriers to the use of ECs. An EC hot line is available in America (011-1-888-668-2528 or 011-1-888-NOT-2-LATE); there is also a web site: http://opr.princeton.edu/ec/.

Table 21. Indications for the use of emergency contraception

Having unplanned sex without protection
Condom slipping/breaking
Dislodgment of a diaphragm, cervical cap, IUD
Missing more than 2 oral contraceptives in a row
Being over 14 weeks from the last Depo-Provera® injection.

Table 22. Reasons for failure to use emergency contraception

1.	Religious/cultural pressures from the family and others
2.	Inability to pay for the services needed to obtain contraceptives
3.	Fear of the absence of confidentiality
4.	Fear of contraceptive side-effects
5.	Failure of health care providers to educate students about ECs
6.	Failure of health care providers 10 prescribe ECs
7.	Fear of liability
8.	Fear it will undermine the youth's use of more efficacious contraception

A copper-containing IUD can be used for EC by inserting it up to five days after unprotected sex anywhere in the cycle or up to five days after post expected ovulation in a female with regular cycle, which inhibits fertilization. It can remain in situ for long term contraception if desired. Mirena IUS (Intrauterine System) should not be used for emergency contraception (124). Contraindications to emergency contraception include existing pregnancy, known acute porphyria, and current warfarin treatment; in the latter situation, anticoagulation may be altered and then coagulation monitoring is necessary (124).

Abstinence is recommended for two weeks after EC administration, while regular contraceptive methods should be started right away, with the exception of Depo-Provera which is best to be delayed for two weeks until pregnancy is ruled out. Pregnancy and sexually transmitted disease testing is recommended two weeks after EC administration. Menstruation usually returns within seven days of the anticipated day. Providing EC information does not lead to youth to unprotected sex habits or decrease the use of regular contraceptive methods (123).

Vaginal ring

The NuvaRing is a soft, flexible, transparent vaginal ring made of an ethylene vinyl acetate copolymer. It has an outer diameter of 54 mm and a cross-section of 4 mm (124). There are two steroid reservoir cores in the ring that provide a daily hormonal release of 15 mcg of ethinyl

estradiol CEE) and 120 mcg of etonogestrel (an active metabolite of desogestrel) (106,107). Etonogestrel implants with depot testosterone is under study asa long-acting male contraceptive (125).

The NuvaRing provides hormone bio-availability comparable to an oral contraceptive, such as Desogen or Ortho-Cept. It is inserted by the female and removed after three weeks. After one week, a new ring is inserted for the next month. If the ring is expelled, it is washed and reinserted; if it is out over three hours, a back-up contraceptive method is recommended until the ring is back in place for seven days in a row. This contraceptive method is popular with college students who are comfortable with their bodies and accept this form of contraceptive technology. Patients should be educated that the ring does not prevent STDs, but provides contraceptive efficacy similar to combined oral contraceptive pills (126, 127). It can be used successfully by adolescent females who are educated about their bodies and this contraceptive method (31,128).

Advantages of the intravaginal ring are listed in table 23 (126-131). Studies have shown that this contraceptive method is well-accepted by adult women and their partners (132-134). Side effects include prolonged menstrual bleeding lasting > 7 days in 25% of cycles, vaginal discomfort, vaginitis, and foreign body sensation. The other side effects noted in those using the NuvaRing are similar to OCP users, including an increased risk of thrombosis. There is usually less irregular bleeding than seen with OCPs. Obesity itself does not affect the contraceptive efficacy, though extremely obese females may have trouble inserting the ring. As ovulation returns during the first cycle after stopping ring use, there is the possibility of pregnancy immediately after discontinuing use of the ring (135).

Table 23. Advantages of the Nuva ring

Good contraceptive efficacy
Continuous hormone release
Gastrointestinal absorption not required
Easily inserted and remove by the wearer
Rapid return toovulation after stopping
Confidential method

VAGINAL BARRIER CONTRACEPTIVES

Barrier contraceptives are listed in table 24 and are potentially good contraceptive methods for those who are highly motivated to avoid pregnancy, are comfortable with their bodies, and can use these methods correctly with each act of coitus (1,2,136). Some adolescents are well motivated and may choose these techniques over others discussed in this article.

Table 24. Vaginal barrier contraceptives

Diaphragm
Cervical cap (Prentif)
Vaginal contraceptive sponge (Today)
Vaginal spermicides
Female condom (Reality)
Male condom

Diaphragm and vaginal spermicides

Table 25 outlines types of diaphragms that are available and table 26 lists contraindications to diaphragm use. Health care clinicians can learn how to fit diaphragms, providing the female with the correct size and instructions on how to successfully use this classic barrier method (137J.The diaphragm is used with vaginal cream or foam, and can be used in conjunction with the condom for increased contraceptive efficacy, as well as increased protection from STDs. Vaginal contraceptives or spermicides include foams, creams, jellies, suppositories, and a film; Table 27 lists advantages of vaginal contraceptives (138-141). Side effects of these agents include vaginal odor and rarely allergic reactions (138). The diaphragm has been associated with an increased risk of urinary tract infections in some women, such as those with diabetes mellitus. Rarely, toxic shock syndrome has occurred in women using a vaginal diaphragm and this

method is contraindicated in women who have a past history of toxic shock syndrome.

Table 25. Diaphragm types

Coil-spring diaphragm (suited for general use) A metal wire is inserted in the rim; the wire is round and spiral-coiled; folds in one plane.
Flat-spring diaphragm (Mensinga) (suited for anteverted uterus and/or a cervix which is long and posteriorly pointed) It is similar to the coil-spring type but is firmer.
Matrisalus diaphragm (Bowbent) (Suited for those with a cystocele or vaginal-wall relaxation) Contains a steel band which is strong and flat; the band is curved and placed in the rim.
Arching-spring diaphragm (Findley) (Suited for those with poor muscle tone or have a cervix which is pointed posteriorly) This diaphragm has a double metal spring rim; an arc is formed when the rim is compressed.

Table 26. Contraindications to the use of the diaphragm

Allergy to rubber or spermicides
Anteversion (severe; forward tilting of uterus)
Complete uterine prolapse
Perineal tears
Retroversion (severe; backward tilting of uterus)
Short anterior vaginal wall
Vesicovaginal (or rectovaginal) fistulas
Toxic Shock Syndrome

Table 27. Vaginal contraceptive advantages

- Allows the pair to share contraceptive responsibility when used with a condom
- Can reduce dyspareunia if present (vaginal lubricant)
- Cost is minimal
- Prescription is not needed
- Provide effective contraception, especially if used in conjunction with condom or diaphragm
- Side effects are few
- Useful for young women with only occasional coitus

Cervical cap

The FDA approved the cervical cap (Prentif cavity-rim cervical cap) in 1988, since it has similar contraceptive efficacy as other barrier contraceptives (1,2). This is a small, latex cap (with spermicide added inside) that is about half the size of a diaphragm; the cap fits around the cervix by suction. Four cervical cap sizes are available, 25% of females cannot be fitted, and some females find it difficult to insert the cap. Cervical cytology screening should be done before or at the time of fitting the cervical cap, since cervical dysplasia has been noted in some females using a cap; the screening is also to be done 3 months after the fitting. Cervical laceration, cervical scarring, and a history of toxic shock syndrome are contraindications to using cervical caps.

Vaginal contraceptive sponge (Today)

This is an over-the-counter. disposable, polyurethane sponge with a concave shape; it can be inserted up to two days before coitus and left in place 6 to 24 hours afterward (1,2). Vaginal malodor, vulvar rash, pruritus, candidiasis, and increased risk for urinary tract infection as well as toxic shock syndrome may develop. Contraceptive efficacy is similar to other barrier contraceptives. It was first introduced to the United States market in 1983, removed in 1994, and again became available in 2005.

Female condom

The female condom is an over-the-counter, polyurethane bag or sheath that is placed in the vagina prior to coitus [1,142, 143]. It was FDA approved as a contraceptive agent in 1993 and in 2005 was made of nitrile and called FC2 with introduction to the US marker in 2007. It is not used with a male condom. The female condom offers some STD protection and provides contraceptive efficacy similar to other barrier contraceptives. Negative aspects of using the female condom include discomfort from inner ring insertion and distracting noise during coitus.

Male condom

Male condoms are recommended to reduce the risk of sexually transmitted diseases (STDs) as well as to prevent pregnancy (144-153). They do not eliminate the risk of STDs and are less effective in preventing the transmission of human papillomavirus (HPV) because of the potential wide spread presence of the HPV infection; condoms can stimulate regression of cervical intraepithelial neoplasia (CIN) and HPV clearance (1,2,150, 151). The contraceptive effectiveness of condoms is equivalent to other barrier contraceptives, if used correctly with each coital act. Advantages of condoms are listed in table 28 while reasons for not using condoms or inconsistent condom use are listed in table 29 (144-147).

The latex condom is preferred, since it is more effective at STD prevention (especially for viral STDs) and has much lower rates of slippage or breakage than noted with the Kraton polyurethane condom **and** lamb **cecum condoms;** many different **kinds** of condoms are available. Latex condoms are associated with increased breakage rates when exposed to high temperatures and/or ultraviolet light; they are also weakened by oil-based lubricants. Latex sensitivities can develop in 7% of the general population and 17-25% of health care workers (148). Health care professionals should present the subject of condoms in a positive, not negative light. Comprehensive education is needed for proper use, as well as role-play scenarios for convincing the partner to use condoms. Adolescents often do not use the condom and need

clinicians to discuss negotiation skills regarding male partner's reluctance (often) to use condoms and encouragement in this regard (1,27,149).

Table 28. Advantages of the condom as a contraceptive

- Allows male to actively take part and share in the contraception of the pair
- Effective contraceptive agent
- Many types available
- May decrease dyspareunia
- Minimal side effects
- Available without prescription
- Decreases risk of sexually transmitted diseases

Table 29. Reasons given for not using condoms as contraceptives

- Condom may rupture
- Cost
- Disrupts foreplay
- Failure of clinicians to recommend condoms
- Failure of pharmacists to make condoms easily available
- Proper technique needed each time
- Reduced penile sensation during coitus
- Refusal of contraceptive responsibility
- Religious beliefs
- Stigma of using a method which is associated with promiscuity and STDs
- Prefers other contraceptive method
- Feel they are low risk for STD acquisition
- Criticism of some that condoms are not 100% effective in STD protection and thus,
- should not be used

INJECTABLE CONTRACEPTIVES

Medroxy-progesterone acetate (Depo-Provera; PMPA) is the main injectable contraceptive available in the United States (1,2,58,154-158). It inhibits ovulation and induces a thin endometrium as well as thick cervical mucus. Depo-Provera is given as an intramuscular dose of 150 mg every three months and has a pregnancy failure rate of only 0.3%. It was approved for the treatment of endometriosis in 1960 and approved to provide contraception in many countries in 1980 (156). FDA approval was delayed until 1992 because of concern over possible increased risk of breast cancer and mutagenic properties even though this contraceptive had been used for many years in other countries; none of these concerns have ever been substantiated. Because Depo-Provera does not contain estrogen, it can be used by women for whom estrogen is contraindicated. A partial list of adverse effects of Depo-Provera are listed in table 30. There is no decreased contraceptive efficacy noted in obese females versus normal weight females, though additional weight gain can occur in some females on this contraceptive (see table 30) (59).

Table 30. Partial list: Side-effects of Depo-Provera

- Acne
- Amenorrhea
- Behavioral changes (depression, anxiety, irritability)
- Breast tenderness
- Decreased bone density
- Dizziness
- Fatigue
- Glucose intolerance
- Hair loss
- Irregular menstrual bleeding
- Nausea
- Weight gain

Bone loss is noted in adolescents on this agent and thus, it should be avoided in those at risk for low bone density, such as adolescents who have chronic renal disease, anorexia nervosa, and possibly those who are wheel-chair bound (1,2,4,62, 154). Depo·Provera users often stop menstruating, especially with prolonged use. Benefits of this contraceptive method include reduced incidence of dysmenorrhea and premenstrual tension syndrome. It may reduce seizure activity in some women who have epilepsy. Fertility can be delayed for one year or more after discontil1uation due to prolonged effect of contraceptive efficacy. Individuals with psychosis and mental retardation who are at risk for pregnancy have been prescribed this injectable contraceptive (89. 90).

In 2000, the FDA gave approval to another injectable contraceptive, Lunelle (5 mg estradiol cypiona1e and 25 mg medroxyprogesterone acetate [MPA/E2C]); it is given intramuscularly every month (every 28-30 days) and has very high contraceptive efficacy. It is available as Cyclo-Provera and as Cyclofem in other countries. Because this injectable contains estrogen, amenorrhea and dysfunctional uterine bleeding (DUB) are less common than noted with Depo-Provera. The mean cycle length is 28 days and there is a predicable bleeding-free interval and less breakthrough bleeding than is noted with OCPs. There also is a rapid return to fertility after discontinuation. The company that manufactures this product recalled it in 2002, because of concerns about the amount of hormones in it. Another progestin-estrogen product that is injectable and available outside the United States is Mesigyna (with 50 mg of norethindrone and 5 mg of estradiol valerate) (154,155).

INTRAUTERINE DEVICES (IUDS)

There are three IUDs which currently are used in the United States: Progestasert IUD, the ParaGard (Copper T380A) and the Mirena IUD (1,2,31,157,159,169). Progestasert IUD was first made available in 1976; it is replaced annually and has an expulsion rate of 2.7%. Paragard was introduced in 1983 and has a lower failure rate than the Progestasert IUD; it is replaced every 8 to 10 years and has a reported expulsion rate of 5%. Paragard may help protect adult women against endometrial carcinoma. There are various other copper IUDs in the world market but

only ParaGard is available in the United States. The IUD is used by 12% of adult women using contraception in the world versus 1% in the United States (160).

The IUD has been linked in the past with inducing increased rates of pelvic inflammatory disease (PID), even though careful analysis notes that the IUD-induced risk is minimal (37). However, litigious concerns have resulted in a situation in which most clinicians in the United States will not insert an IUD in a female unless she is at a minimal age (often 21 years of age), is in a mutually monogamous relationship, has no history of PID or ectopic pregnancy, and has demonstrated her fertility.

The Mirena IUD (levonorgestrel-containiog IUD; LNG-IUD) is a second generation of steroid-releasing IUDs; it has a 32 by 32 mm Nova T-shaped polyethylene-barium sulfate frame (1 1/4" tall and wide, made of plastic) with a rervoir around the vertical stem containing silicone and 52 mg of levonorgestrel (161). Two threads for removal are attached to the end of the stem. It is packaged in a sterile state inside an insertion device that is disposable.

This IUD releases 20 mcg of levonorgestrel per 24 hours over the first five years of use; the levonorgestrel released decreases to 10 μg/day after five years. Concentrations in the plasma stabilize to 150-200 pg/ml, less than noted with oral contraceptives or Norplant. Mirena has been available in Europe for over 10 years and has been used by over two million women worldwide (161). The Mirena IUD was approved by the FDA in 2001 for five years use in the United States, though it is used in Europe for seven to 10 years before replacement is recommended. It is a highly effective contraceptive, with a failure rate of 0.2% in the first year and 0.7% at five years (161-164). It is inserted before day seven of the cycle and is not effective if inserted post-coitally. A newer insertion device allows easy insertion with minimal uterine perforation risks. It exerts a local effect on the endometrium, as well as the cervical mucus, and can initially lead to systemic effects (165).

Table 31 lists the contraceptive mechanism of IUDs (166). Ovulation can continue and amenorrhea may develop because of endometrial thinning. Table 32 lists the side effects of the Mirena IUD. The most common side effect is menstrual bleeding; there is increased bleeding and spotting during the first 3 to 6 months after insertion, but this usually decreases thereafter. This IUD has been used to reduce heavy menstrual

bleeding in adult females because up to 90% of menstrual blood loss eventually may be decreased (167-170). The use of an IUD in females with mental retardation has been identified (89,90). Table 33 lists the benefits of the Mirena IUD (169). Contraindications to Mirena use include active pelvic inflammatory disease, prosthetic heart valves, history of subacute bacterial endocarditis, and distorted uterine cavity. Obese females have an increased incidence of dysfunctional uterine bleeding and endometrial hyperplasia, making the Mirena IUD a good contraceptive choice for obese females needing contraception; there is no decreased contraceptive efficacy due to obesity (58,59).

Table 31. IUD contraceptive mechanisms

1. Prevents fertilization
2. Interferes with ovum development
3. Interferes with sperm movement and ability to penetrate ovum
4. Inhibits sperm survival
5. Helps prevent egg release
6. Thickens cervical mucus

Table 32. Mirena side effects (160)

Common
- Initial increased menstrual bleeding
- Abdominal pain

Uncommon
- Acne/other skin problems
- Back pain
- Breast tenderness
- Headache
- Nausea
- Mood changes

Rare
- Hypersensitivity reaction
- IUD becomes embedded in myometrium
- Perforation ofuterus or cervix

IUD inserted during pregnancy (increases pregnancy complications: Miscarriage, sepsis, premature labor, premature delivery)
Development of intrauterine pregnancy after insertion; must remove IUD

Table 33. Benefits of Mirena IUD

1. Effective contraception
2. Eventual reduction in menstrual flow (90%)
3. Frequent amenorrhea
4. Decreased dysmenorrhea
5. Decreased premenstrual syndrome
6. Very low rates of infectious complications
7. May decrease PID incidence in the long run
8. Decreases ectopic pregnancy (2/10,000)
9. Avoids use of estrogen
10. No significantly increased pregnancy risk if on anti-epileptic or other Enzyme-inducing medications
11. Rapid return to fertility (80% within one year of removal)

IMPLANTS

Norplant is a long-acting, levonorgestrel-containing contraceptive designed to be implanted subcutaneously in the upper arm (1,2). Each of the six matchstick-sized capsules is 34 mm long and 2.4 mm in diameter and contains 36 mg of levonorgestrel. Contraindications to its use include active thrombophlebitic or thromboembolic disorder, undiagnosed or abnormal genital bleeding, known or suspected pregnancy, acute liver disease (including. benign or malignant liver tumors), and known or suspected carcinoma of the breast. It was withdrawn from the United States market in 2000.

Implanon contains one rod (vinyl ethylene acetate polymer) that contains etonogestrel, while the Jadelle implant (Norplant II) has two silastic rods with levonorgestrel (15,171,172). These two implants are FDA-approved for three years. There is no decreased efficacy with

obesity, though some have lower etonogestrel levels (59). Some weight gain may be noted with both implants.

STERILIZATION

Sterilization (female sterilization. vasectomy [males]) is not normally recommended for adolescents, but has been suggested for youth with such issues as intellectual disability/mental retardation or schizophrenia. However, it remains a controversial issue in the United States and is generally only appropriate for some adult females (173,174).

NATURAL FAMILY PLANNING

Natural family planning (fertility awareness; physiologic methods) is the method based on recognition of ovulation timing. Usually, there is a combination of daily temperature recording, cervical mucus observation, and other symptoms (175). General information about the calendar method is good education for youth and can help them use other contraceptives more effectively; however. adolescents are usually not motivated enough to correctly use natural family planning and it has a high failure rate in youth (176).

COITUS INTERRUPTUS

Coitus interruptus is a method used by many youth and is one of the oldest contraceptive methods. However, it is not a recommended contraceptive method for adolescents because of its high failure rate-19% per annum (1,2).

CONCLUSIONS

Contraception is an important concept for sexually active adolescent females to understand who do not wish to become pregnant. This chapter has reviewed important, effective, and safe contracep1ive methods that can be used by female youth. Promotion of sexual responsibility should be the charge of health professionals caring for adolescents and young adults. The framework of sexual responsibility includes prevention of unwanted pregnancy and S1Ds. The clinician should provide contraceptive advice chat elicits important pertinent information such as age and sex of her partner as well as last unprotected sex and menstrual period. Education can be given regarding appropriate information about pregnancy and STD risk as well as contraindications to contraceptive methods (17,177,178).

Youth who have chronic illness and are sexually active should also be provided with safe, effective contraception, as reviewed in this chapter. Though abstinence is a highly recommended method of concraccption, coitus interuptus and natural family methods are not, because of their high failure rates. Care must be utilized in prescribing an IUD in the adolescent or college student, because of the litigious overlay of concern for pelvic inflammatory disease, as reviewed in the IUD section of this discussion. Finally, sterilization is a method of contraception normally not recommended for youth.

ACKNOWLEDGMENTS

This chapter is an adapted version of an earlier publication (Greydanus DE, Rimsza ME, Matytsina L. Contraception for college students. Pediatr Clin North Am 2005;52:135-61) and adapted with permission.

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