MANAGING CONTRACEPTIVE PILL PATIENTS

Millennium Edition

by Richard P. Dickey, MD, PhD

medical publishers

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Chairman, Medical Advisory Board, Louisiana State Family Planning Program, F.A.C.O.G.; Board Certified Obstetrics and Gynocology and Reproductive Endocrinology and Infertility; Clinical Professor of Obstetrics and Gynocology, and Chief Section of Reproductive Endocrinology and Infertility, Louisiana State University School of Medicine, New Orleans; Medical Director, The Fertility Institute of New Orleans.

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Preface

The tenth ("millennium") edition of *Managing Contraceptive Pill Patients* (*MCPP*) is dedicated to the memory of Dr. John Wells, co-founder of Creative Infomatics (currently EMIS, Inc.), who first adapted the center index format for use in a medical publication. Even though it is anticipated that, in the 21st century, all medical information will be available on the Internet, physicians and medical personnel will still need an instantly available printed guide to oral contraceptive pill differences and medical management of side effects.

The length of the tenth edition has been reduced by removing redundant or out-of-date information and references, most notably in the sections on the cardiovascular system and effects of OCs on pregnancy. The reader who is interested in the older information may find it on the Internet at "9thedition.www.emispub.com". Since the first edition, published in 1977, *MCPP* has introduced many ideas about oral contraceptive use that have become part of the U.S. FDA's required package insert. These include the use of the lowest doses of estrogen and progestin consistent with effectiveness, the concept that the net effect of an OC depends on the type and/or amount of progestin and on a balance between the estrogen and progestin components, a listing the benefits of OC use, and inclusion of information about the relationship of estrogen to cardiovascular disease. The "pill book" remains the only single source for information about real differences among OCs in estrogenic, androgenic, progestational, and endometrial (breakthrough bleeding) potencies and management of side effects in relation to these differences.

The second printing of the 10th edition of *Managing Contraceptive Pill Patients* follows shortly after FDA approval for sale in the U.S. of Lunelle™, a once-per-month contraceptive injection, and of Mifeprex™ (mifepristone, RU 486). Information about Lunelle™ has

been added to Section #23; its use for emergency contraception within 72 hours of intercourse is presented in Section #24. Mifeprex™, in combination with misoprostol, is indicated for the medical termination of pregnancy through the 49th day from the last menses.

R.P.D.
New Orleans
January 3, 2000

Readers are invited to send suggestions for changes and new information they believe should be included in *Managing Contraceptive Pill Patients* to the author in care of the publisher by e-mail at http://www.emispub.com or by FAX to 214/349-2266. If the information is used, the sender will receive a free copy of the next printing. As always, new information is added at the time of each new printing.

Introduction

Popularity of OC Use

Oral contraceptives (OCs) are the most widely used and successful method of reversible birth control in the world. Since their introduction in 1960, the acceptance and popularity of OCs have continued due to their:

- High rate of effectiveness
- Simple method of use
- Ease of discontinuance
- Rapid reversal of effects after discontinuance
- Beneficial effects on the menstrual cycle

Risks of OC Use

The risks associated with OC use (see Table 2) are low compared to the risk to life associated with pregnancy, except in women who:

- Smoke cigarettes and are older than age 35
- Have Leiden factor V mutation (Ref 350)

Reducing Risks

Nearly all the excess risk of death due to OC use can be attributed to cardiovascular disease. The increased risk of cardiovascular disease may continue for a number of years after OCs are stopped. Both long- and short-term risks may be reduced if women:

- Use OCs containing smaller and less biologically active amounts of estrogen and progestin
- Are carefully screened and those at high risk advised to choose other contraceptive methods
- Recognize and report clinical symptoms that may precede serious illness early in their occurrence

Health personnel are often faced with the dilemma of choosing between an OC with high hormone activity in order to assure regular menses and continued patient use and an OC with low hormone activity in order to reduce side effects. The choice of OC must be individualized for each patient.

OC Patient Management

The essential elements for good management of OC patients are:

- Knowledge of the contraindications to OC use, both absolute and relative (see Section #19)
- Knowledge of the causes of common side effects (see Section #4)
- The ability to recognize potentially serious illnesses as soon as they occur (see Table #11)
- Access to accurate information about biological activity differences among OCs (see Section #3)

Using This Text

Clinical information about the frequency of most of the known OC side effects and their usual outcomes is provided in this text as well as a recommended plan of their management. In many cases, the recommended course of management is to switch patients to OCs with different levels of one of the four major biological activities. Table 5 lists these categorical activities and should prove helpful to clinicians as they choose OCs.

The activity profiles of various OCs are especially advantageous for the selection of an initial OC (see Section #21). The number of women who can successfully use OCs can be increased if the initial OC is selected to avoid particular side effects. Patients can later be switched to different OC formulations (determined according to their biological activity rankings) if side effects occur.

Recommendations for selecting an initial OC are summarized in Table 7. OCs listed in Table 8 are categorized into 13 groups according to their estrogen amounts and progestational, androgenic, and endometrial activities. OCs from Groups 1, 2, and 5 through 8 have 35 mcg or less estrogen and the lowest androgen activities. OCs in these groups may reduce immediate and delayed cardiovascular side effects.

Approximately 90 percent of patients should be able to take at least one of the OCs containing less than 35 mcg estrogen without experiencing symptoms of menstrual irregularity after the third cycle of use.

1. #1 Benefits of OCs to Reproductive Health

Benefits of OC Use

Women receive significant benefits during and after discontinuing OC use (see Table 1). These benefits include:

- Avoidance of pregnancy-related complications (Ref 242)
- Reduced premenstrual symptoms and menstruation-related anemia (Ref 284, 355, 368)
- Reduced incidence of endometrial and ovarian cancers (Ref 32, 38, 44, 165, 167, 295, 303, 304, 372, 373)
- Reduced incidence of many common diseases (Ref 192, 284, 377)
- Reduced incidence of gynecological diseases that cause infertility (32, 88, 89, 116, 150, 284, 297)

It is estimated that, for every 100,000 OC users, the following pregnancy-related conditions (Ref 242) are avoided:

- 117 ectopic pregnancies
- 10,500 spontaneous abortions
- 10,407 term pregnancies requiring Cesarean sections

Complications of these conditions are the leading causes of maternal deaths in young women.

Additionally, breast biopsies are reduced in OC users (Ref 33, 238, 239, 240, 241, 285).

An important beneficial effect of OCs for women who want to delay child-bearing is the protection provided against four of the most frequent causes of infertility:

- Endometriosis (Ref 32, 41, 88, 284, 364)
- Pelvic inflammatory disease (PID) (Ref 89, 297)
- Ovarian cysts (Ref 41, 285, 355, 403)
- Uterine fibroids (Ref 41, 284)

These diseases account for approximately 50 percent of all infertility due to a female factor and 90 percent of infertility that requires surgical treatment.

Safety of Use

Combination OCs are equal to or surpass other contraceptive methods in safety compared to pregnancy until age 35 for smokers and throughout life for nonsmokers (see Table 2) (Ref 263, 264, 335, 338, 339). To minimize risks, older women should be cautioned to take the lowest dose formulation that maintains menstrual regularity.

All of the increased mortality associated with OC use is related to cardiovascular disease (CVD). OC use is safe throughout reproductive life in women who:

1. Have no cardiovascular risk factors, i.e.:
   - Hypertension
   - Obesity
   - Hyperlipidemia
2. Have no family history of CVD
3. Do not smoke
4. Use regimens containing an average estrogen dose of less than 50 mcg
5. Do not have Leiden factor V mutation (Ref 350)

A further reduction of the hazards of combination OCs may be achieved with:

- Progestin-only OCs
- Progestin injections
- Progestin implants
- Progestin-containing IUDs
- OCs with progestational and androgenic potencies less than or equal to 0.5 mg of norethindrone

#2 Composition and Effectiveness

2.

OC Composition

OCs are composed of synthetic estrogens and progestins (compounds with progestational properties) (Ref 64, 68).

Two synthetic estrogen and 12 synthetic progestin possibilities are available, although not all progestins are available in all countries. Estrogens and progestins vary in their biological activities (see Table 3).

The compositions and identifying characteristics of OCs available in the U.S. are shown in Table 4. OCs also contain inactive ingredients that act as fillers and preservatives. Rarely, women are allergic to the nonsteroidal contents (shown in footnotes of Table 4). When an allergic reaction occurs, it is most often due to lactose. There are only six combination OCs that do not contain lactose.

In combination OCs, the types and doses of estrogen and progestin remain constant during the 21 days that tablets are taken, though the doses and ratios of estrogens and progestins vary from one preparation to another. Many combination OCs are also available in 28-day packages, which contain 21 active and seven inert or ferrous fumerate tablets.

In biphasic and triphasic OCs, the dose of the progestin or estrogen component changes during the cycle in an attempt to duplicate the pattern of the ovulatory menstrual cycle.

Sequential preparations have been discontinued in the U.S. and Canada because of a possible increased risk of endometrial cancer. These regimens included 14 to 15 days of estrogen in doses above 50 mcg, followed by five to six days of estrogen and progestin.

Progestin-only OCs contain no estrogen and are taken continuously. They are available in 28- and 42-day packages.