Manual of Obstetrics

Diagnosis and Therapy

Edited by
Kenneth R. Niswander, M.D.

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Preface

Manual of Obstetrics has been written with the house officer in mind. He or she needs a quick source of clinical data in easily retrievable form to help in the care of the obstetric patient. We hope that this book will satisfy that need. The writing has been done primarily by house officers, who know from firsthand experience what information a neophyte requires to provide good care for the obstetric patient. We hope the information these young physicians have packed into these few pages will serve the practitioner well. The completeness, yet succinctness, of their writing, frequently their first experience in authorship, has been a source of pride to their elders. I have again and again been reminded to what extent we constantly learn from the young.

As far as possible, we have tried to report our own experience, supplemented where necessary by reference to the literature. We have emphasized diagnosis and treatment at the expense of detailed discussions of the pathophysiology of disease. This is not an atlas of obstetric procedures. We have tried always to keep the welfare of the fetus in mind, but not at the expense of maternal well-being.

Many colleagues, some of whose names do not appear in the table of Contents, have contributed their time by reviewing individual chapters. We would like to thank Dr. Eugene Abravanel, Dr. James Castles, Dr. Pierre Dreyfus, Dr. Frederick Hanson, Dr. Lester Hibbard, Dr. Jon Hirasuna, Dr. Garrett Lee, Dr. Jose Nabres, Dr. Richard Oi, Dr. Karen Poirier-Brode, Dr. Robert Walters, and Dr. John Watson-Williams. We are greatly indebted to Dr. Robert Goodlin for the intellectual milieu he created on our Service and for the thoughtful approach to obstetrics with which he has imbued our young house officers.

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Contents

I

Pregnancy

1

Contraception, Abortion, and Sterilization

Kenneth R. Niswander

CONTRACEPTION

Fertility control has become an increasingly important facet of the delivery of health care. While contraception has been practiced for a very long time, the recent development of fertility control agents that are not only more effective but also more convenient than earlier methods has broadened the choice of agents available to couples. The wide range of available agents makes it possible to give good contraceptive advice to almost every patient who desires it. Good advice to patients is providing them with good information and allowing them to make an intelligent choice among the many methods available. They will want to know the effectiveness, the shortcomings, the dangers, and the expense of the devices or drugs from which they can choose.

I. Effectiveness. The effectiveness of a contraceptive method can be described in two ways: **Theoretic effectiveness** is reached when the method is used without error and exactly according to instructions. **Use effectiveness** describes the predicted success rate when the method is used by a population with varying degrees of motivation and a wide range of skills. While an individual patient may approach theoretic effectiveness with a particular contraceptive method, it is better to quote both use effectiveness and theoretic effectiveness when counseling a patient.

The theoretic and the actual use effectiveness rates for most available agents are listed in Table 1-1. The figures listed are the number of pregnancies that will occur during the first year of use per 100 nonsterile women initiating the method. It can be seen that combined oral contraceptives are virtually 100-percent effective theoretically but that the actual use effectiveness reported in various series is 4 to 10 pregnancies. The diaphragm and spermicide have a theoretic effectiveness of 3 pregnancies and an actual use effectiveness of 17 pregnancies. Thus, the highly motivated patient may get better protection from a diaphragm than would an average patient with oral contraception. It should be noted that of 100 sexually active women using no contraceptive method, 90 will become pregnant during the first year of exposure.

II. Available agents

A. Oral contraceptives. Oral contraceptives are potent steroid medications that prevent pregnancy primarily by inhibiting ovulation. Changes in other reproductive physiologic aspects induced by the agent may, in themselves, prevent pregnancy; for example, the pill containing a low-dose progestin alone prevents pregnancy by altering endometrial metabolism and the type and amount of cervical mucus as well as by inhibiting ovulation, since ovulation may occur in 50 percent of such patients. Alterations in tubal motility may also contribute to the pregnancy protection.

Either an estrogen or a progestin alone in a sufficiently large dose will prevent ovulation. The medications are usually combined, since the dose of either medication alone necessary to prevent ovulation usually causes an unacceptably high rate of breakthrough bleeding or other undesirable side-effects.

Table 1-1. Approximate Failure Rate of Various Contraceptive Techniques

Technique	Pregnancies per 100 Woman-Years	
	Theoretic Failure Rate	Actual Use Failure Rate
Oral contraceptive (combined)	0.34	4–10
Condom + spermicidal agent	Less than 1	5
IUD	1–3	5
Condom	3	10
Diaphragm with spermicide	3	17
Spermicidal foam	3	22
Coitus interruptus	9	20–25
Rhythm	13	21
Chance (sexually active)	90	90

The most commonly prescribed medications contain both an estrogen and a progestin. With this combination therapy, a tablet containing both an estrogen and a progestin is taken for 20 or 21 days, beginning on day 5 of the initial menstrual cycle. The primary antifertility effect is mediated by the progestin, which prevents ovulation as well as effecting changes on the endometrium and on the cervical mucus. The estrogen is added principally to decrease the number of days of vaginal bleeding experienced by the patient. Recently, a tablet containing only a progestin has been marketed. The antifertility effect of this drug is somewhat lower (about three pregnancies per 100 woman-years) than the combination pill, and the number of days of bleeding is substantially increased. The major advantage of this pill is the lack of side-effects caused by estrogen, some of which may be very serious, as described below.

1. **Effect of oral contraceptives on various organ systems.** In addition to their antifertility activity, oral contraceptives exert effects on many other organ systems. These effects are important for a number of reasons. Certain organ function tests are substantially altered by contraceptive medication, thus complicating the diagnosis of disease in these organs during contraceptive ingestion. Contraindications to the use of pills are frequently based on the effect of the pills on a particular organ system. The side-effects of the pills may result from an undesirable action of the drug on certain organs.

   a. **Effect on reproductive organs.** Ovulation is prevented, thus decreasing the number of patients with a functional ovarian cyst. Combined therapy usually produces a secretory effect on the endometrium, and this may proceed to marked glandular suppression and amenorrhea. The effect of combination pills on leiomyomas of the myometrium is variable, but rapid enlargement is sufficiently common to make the presence of leiomyomas a relative contraindication to oral contraceptive use. The cervix may exhibit a polypoid hyperplasia, but there is no evidence that oral contraceptives increase the risk of development of carcinoma of the cervix. Breast tenderness is a well-recognized side-effect of oral contraceptives, and this is caused primarily by the estrogen in the medication. Oral contraceptives decrease the incidence of benign breast disease. If given during the postpartum period, they may decrease milk production and they cross into the milk, which may or may not be important.

b. Effect on other endocrine organs. Estrogen increases the amount of circulating binding globulins, thus increasing the total amount of bound circulating cortisol and thyroxin. Since these increases are in the bound fraction of the hormone, there is no recognized change in either adrenal or thyroid function in patients maintained on the medications.

Some patients experience a rise in plasma insulin levels, followed soon thereafter by a rise in the fasting blood glucose or by an abnormal glucose tolerance test. In most patients, these tests revert to normal following the discontinuation of the medication. Whether oral contraceptive medication merely identifies the patient in whom diabetes mellitus is likely to develop in later life or is actually diabetogenic is uncertain. The effects on carbohydrate metabolism are apparently mediated by the progestin content of the pills or by a synergistic action between the estrogen and progestin components.

Inhibition of ovulation by oral contraceptives is induced primarily by the progestin component of the medication and is mediated apparently by an inhibition in the release of luteinizing releasing factor (LRF) from the hypothalamus. If the progestin component is too high, prolonged amenorrhea during medication or postmedication amenorrhea may result. This effect is discussed in section **2.a.(4)** below.

c. Effect on other organ systems. A minimal increase in certain blood-clotting factors (Factors VII, IX, and X, fibrinogen) has been reported with oral contraception, but these changes are probably of no clinical importance. The hypertension that occurs in a small number of patients treated with oral contraceptive medication may be mediated through changes in the renin-angiotensin system. As discussed in section **2.a.(3)**, discontinuation of the medication usually results in a return of the blood pressure to normal. Some liver function tests (e.g., bromsulphalein excretion) may show levels that are elevated, but this change is of no known clinical significance. Cholestasis may occur with the medication just as it may occur during pregnancy. Hyperpigmentation of the skin of the face in a butterfly distribution (chloasma) is seen in a few patients taking oral contraceptives. This may not completely disappear after discontinuation of the medication.

Whether certain side-effects of the medications—nausea and vomiting, depression, loss of libido, and headache—are caused by effects on the central nervous system (CNS) is not known. While some of these symptoms are undoubtedly mostly emotionally induced, headache may be a precursor of cerebrovascular accident (CVA), and persistent headache is reason to discontinue the medication.

2. Side-effects. Since oral contraceptives are potent agents capable of exerting effects on virtually all organ systems, it is not surprising that side-effects are common. While most are merely annoying, a few are life-threatening. Counseling of the patient who chooses oral contraception obviously must include a description of the serious complications of the medication, with an estimation of the risk that must be taken by that individual patient.

a. Major complications

(1) Vascular complications. An increase in the risk of **superficial and deep venous thrombosis** and **pulmonary embolism** in women being given oral contraceptives has been well established by a number of retrospective epidemiologic studies [1, 2]. These case control studies were confirmed by cohort studies that showed the risk of venous thromboembolism in oral contraceptive users is about 3 to 11 times as great as in nonusers. The difference is greatest if only

the diagnosis of idiopathic deep venous thrombosis or pulmonary embolism is used. The risk of superficial venous thrombosis seems less affected by the oral contraceptive medication.

There is evidence that the estrogenic component of the oral contraceptive is responsible for this increase in the risk of venous thromboembolism [3]. This same report also confirmed that there is apparently a marked excess of cases associated with higher doses of estrogen, suggesting a dose relationship. There seems to be no association between duration of oral contraceptive use and venous thromboembolism, and the increased risk disappears shortly after discontinuation of the medication.

(a) **Thrombotic stroke** apparently is increased about sixfold in patients on oral contraceptive medication [1, 4, 5]. The risk is also correlated with the estrogen content of the oral contraceptive.

(b) **Myocardial infarction.** The risk of nonfatal infarction is also increased about fourfold in patients being given oral contraceptive medication [6]. Cigarette-smoking increases this risk substantially, as does a history of preeclamptic toxemia and hypertension or type II hyperlipoproteinemia. A retrospective study of fatal cases of myocardial infarction produced similar findings.

A very crude estimate of the effects of oral contraceptives on the risk of myocardial infarction suggests that the risk of myocardial infarction attributed to oral contraceptive use might be reduced if other predisposing factors (cigarette-smoking, diabetes, history of hypertension) were not present [6].

(2) **Tumors**

(a) **Liver tumors.** In spite of the absence of any prospective study, it is now widely accepted that there is a link between oral contraceptive medication and tumors of the liver, notably focal nodular hyperplasia or hepatic adenoma [7]. Sixty of the first 78 cases of liver tumor recorded with the Registry of Tumors were of these varieties. The histologic appearance of the tumors is similar, except that the adenoma is a solid tumor while focal nodular hyperplasia consists of multiple superficial firm nodules.

The symptom of abdominal pain is probably secondary to stretching of the liver capsule by the tumor. Evidences of intraperitoneal bleeding may be present, as may nausea and vomiting. The patient may palpate the tumor herself. No reliable screening technique that might identify patients at risk is currently available. While no universally dependable diagnostic aid is available, radionuclide scan is frequently positive, as is B-scan. Computed axial tomography (CAT) scans are new but probably will prove to be highly useful. A definitive diagnosis is made by tissue specimen, obtained either by percutaneous liver biopsy or by open biopsy.

The best treatment is uncertain. Extensive resection has been used in the past, but the biologic behavior of the tumors is unknown. There is some evidence that these tumors may regress after withdrawal of the oral contraceptive medication.

(b) **Cancer of the breast and endometrium.** Sufficient data to establish an association between oral contraception and subsequent cancer of the breast and/or endometrium are un-

available. In view of the recent evidence that an increased risk of endometrial or breast cancer may occur among perimenopausal women who use exogenous estrogens, a relationship between oral contraception and tumors of these organs must be considered a good possibility.

(c) **Cervical and ovarian neoplasia.** Retrospective studies have demonstrated no evidence that oral contraception is related to cervical or ovarian neoplasm [8]. A recently completed prospective study by Peritz and associates has noted a positive association between oral contraceptive use and an increased incidence of cervical neoplasia [9]. The matter is still unsettled.

(3) **Hypertension.** It seems well established that a slight increase in mean systolic and diastolic blood pressure occurs in women being given oral contraceptive medication. The increase in blood pressure is severe in a rare patient. Spellacy has demonstrated that this rise in blood pressure is caused by the estrogenic component of the pills [10]. The hypertension does not seem to be dose-related and may occur as early as 1 to 3 months or as late as 8 years after the initiation of contraception. The etiology is unknown, and Weinberger feels that changes in the renin-angiotensin-aldosterone system cannot fully explain the estrogen-induced hypertension [11]. Cessation of estrogen therapy results in a decline of blood pressure to normal levels in most patients. Whether the oral contraceptive identifies a group of women likely to develop subsequent hypertension or whether the hypertension is only a drug-related phenomenon is unknown.

(4) **Postmedication amenorrhea.** Amenorrhea of more than 6 months' duration occurs in 0.2 to 0.8 percent of contraceptive pill-users after discontinuation of the drug [12]. In one study of postpill amenorrhea, 43 percent of the patients gave a prior history of oligomenorrhea [12]. This was significantly higher than the 11 percent found in all infertile patients. Similarly, 57 percent of these patients experienced galactorrhea, a much higher incidence than was expected. Only 37 percent of the women with postpill amenorrhea alone or postpill amenorrhea with galactorrhea ovulated when treated with clomiphene citrate, a much lower rate than achieved in other women with secondary amenorrhea. Women who discontinue oral contraception apparently are not more likely to experience pituitary tumors with the usual symptoms of amenorrhea and galactorrhea [13].

b. **Minor side-effects.** Certain minor but troublesome side-effects are associated with contraceptive pill ingestion. These symptoms include vaginal bleeding, nausea and vomiting, weight gain, and other minor annoyances.

(1) **Intermenstrual bleeding** occurs less frequently with estrogen-dominant pills than with progestin-dominant medication. Bleeding that occurs early in the cycle is usually related to the low estrogen content of the contraceptive medication. Bleeding that occurs late in the cycle may be a result of a deficient progestin content of the medication. A change to a more appropriate medication may be tried, although the complaints usually disappear after one or two cycles.

(2) **Nausea and vomiting** are related to the high estrogen content of the pill. A pill with a lower estrogen content or a lower estrogen-progestin ratio may be tried.