

creasing the daily dose is of value in controlling the bleeding. If a menstrual period is missed completely the patient must resume the medication seven days after taking the last tablet. When the oral contraceptive is discontinued it is important to advise the patient that her first menstrual period may be delayed as long as two or three weeks after the expected date. The patient should remain accessible to medical supervision for control of any side effects.

Further reductions and modifications in dosage schedule are being introduced. One variation is sequential therapy—administration of an estrogen alone for 15 or 16 days followed by the progestin-estrogen combination for the remaining five days of the 20 or 21 day schedule. Another regimen which consists of taking a pill every day, is now also available. Under this regimen a "combined" pill is taken for 21 days and a placebo for the remaining seven days.

Not yet approved by the FDA for other than research in this country (but already marketed in several countries abroad) are two new methods, the so-called "minipill," consisting of a minute dose of a progestin only, and taken every day of the month and the once-a-month, and once-every-three-month injectable. The once-a-month injections consist of the same estrogen-progestin combination as are contained in the combined pill, injected intramuscularly so that the ingredients are only slowly released into the system. The once-every-three-month injectables, like the minipill, consist of a progestin only. Neither of the progestin-only contraceptives appears to consistently suppress ovulation in most cases. Their contraceptive effect is thought to depend primarily on the production of a hostile cervical mucus and effects on the endometrium.

Mechanism of Action

The mechanism of action of the currently approved oral contraceptives is primarily that of ovulation suppression. Other mechanisms which may contribute to the effectiveness of this method include an acceleration of endometrial development, alteration of tubal factors, and the production of a hostile cervical mucus. According to the World Health Organization, "...it seems likely that different types of compound, or even the same compound at different dose levels, may act in different ways, and that the individual compounds and their combinations may exhibit multiple mechanisms of action. There is also evidence to suggest that the mode of action of contraceptive steroids in the first one or two cycles of use differs from that in later cycles... Inhibition of ovulation is not essential to the antifertility effect of steroids. For example, the continuous administration of low doses

of progestogens does not consistently inhibit ovulation, although it offers a very high degree of protection against conception. The way in which fertility is inhibited in the presence of ovulation is incompletely understood..."

Effectiveness

Taken according to instruction the combination oral contraceptives now available are virtually 100 per cent effective. The report of the Advisory Committee on Obstetrics and Gynecology of the FDA, August 1, 1966, states: "The efficacy of the combined agent is exceptionally high. The more recently introduced sequential regimens are also highly effective in controlling fertility although to a slightly lesser degree. Present evidence indicates that the frequency of pregnancies occurring with the patients on sequential medication remain unchanged over the two and one half year period, thus supporting the contention that tolerance to or escape from the medication probably does not occur."

Acceptability

Clinical studies have demonstrated that patient tolerance of this method of contraception varies somewhat with the different products and dosages, and is also dependent upon other factors such as culture, motivation, income, and level of education. In general, the pills have been found acceptable to between 70 per cent and 90 per cent of patients. Secondary benefits of the oral method have also been reported. The menstrual cycle is regulated in practically all women and is accompanied by a decrease in the amount of menstrual flow and an improvement, in many cases, of pre-existing dysmenorrhea.

According to the 1965 National Fertility Study, conducted by Professor Charles F. Westoff of Princeton and Professor Norman B. Ryder of the University of Wisconsin, the overall dropout rate from the pill among all U.S. women for all reasons is about three to four per cent a month over the first three months, and one to two per cent in subsequent months. About 80 per cent continue with the pill for at least one year; and, the study found, some two-thirds of women who had started with the pill in 1960 were still using it five years later. Rates of discontinuance appear to be higher among women of lower educational attainment. Most who discontinue drop out because of side effects such as nausea or intermenstrual bleeding. A Population Council report indicates that about 13 million women are using oral contraception as of July, 1967, 6.5 million of them in the U.S. (representing nearly one-fourth of married women of childbearing age). The report found drop-out rates for the pill considerably higher in developing countries studied than in the U.S. In half the countries studied more than half of those women initially ac-