Contraception update

Part 2: A practical up-to-date review for choosing an oral contraceptive

— K E Sapire

Summary

In the selection of oral contraceptives, an understanding of the two basic types of progestogen and estrogen is important. Further, a knowledge of the woman's tendency/risk for various problems such as acne, high blood pressure and pre-menstrual tension are important in deciding on the best product for the person.

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Selection of oral contraceptives (OCs)

Fundamentally there are two types of progestogens. Estranes contain or are metabolised to norethisterone, and gonanes that contain norgestrel, levonorgestrel or its close relative, desogestrel. Gonanes (except for desogestrel) have a mild androgenic activity and no discernible estrogen activity, and they have an anti-estrogen activity which reduces the metabolic changes induced by the estrogen component. Conversion of estranes to biologically active estrogen occurs to some extent, but in low-dose pills this estrogenicity is neglible. It is doubtful if any progestogen is 'estrogenic' or 'androgenic' in the doses recommended today. There is still controversy regarding the potencies of progestogens and their relevance to adverse effects in clinical use.

Triphasic formulae are a response to the evidence that the adverse effects of OCs are dose related. The increase in hormones allows the lowest quantity of both estrogen and progestogen to be used. They imitate the pattern of the ovulatory cycle, and this probably explains the improved cycle stability. The histology of the endometrium is similar to the ovulatory pattern and different from that during the use of uniform or monophasic low-dose pills where some women complain that they "bleed when they shouldn't and don't bleed when they should". The effects on metabolism and blood pressure and coagulation are minimal with triphasic pills, and cycle control is usually good after the first 3 months. However, mastalgia and premenstrual tension are more common as the progestogen dose is extremely low and there is an estrogen dominant ratio. Therefore, in women with premenstrual tension, monophasic low-dose pills are preferred.

The formula for selection of OCs has thus become clearer. Women without contra-indications or risk factors should use low-dose triphasic pills. If side effects (e.g. headache) occur in the gonane group (Triphasil, Logynon) a change should be made to the estrane group (Trinovum), or vice versa. If premenstrual tension becomes a problem, a monophasic low-dose pill (Nordette, Brevinor, Restovar or Marvelon) should be used. If breakthrough bleeding persists after 3 months, a higher-dose pill (Ovral or Minovlar) should be used for 3-6 months. Then revert back to a triphasic pill in the same group.

The low-dose monophasic and triphasic oral contraceptives inhibit ovulation and are just as *effective* as higher-dose pills, but as blood levels are critical the margin for error has narrowed and omissions are more likely to result in pregnancy. Patients should be advised to take the pill morning or evening and associate it with something they cannot forget to do, like brushing their teeth. Forgotten pills are especially dangerous at the beginning or end of a pack, as this lengthens the pill-free time, and in some women ovulation may occur, and this could result in pregnancy. If a pill is forgotten for more than 36 hours, additional precautions must be used for at least 14 days.

The proven acceptability, efficacy and safety of OCs suggest that they will still be with us for a long time

Amenorrhoea during treatment is rare with low-dose pills. There is no contra-indication to continuing OCs, provided pregnancy is excluded.

"Post-pill amenorrhoea" must be investigated as for secondary amenorrhoea, as the association with pill use is not thought to be causal.

Subsequent fertility: There is no evidence of permanent sterility after the use of OCs. There is often a

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6-12 week delay in resumption of ovulatory cycles after discontinuing OCs, but there is no evidence that the pill affects future reproduction adversely or favourably, and normal fertility rates occur by 3 months. There is no association with return of fertility and duration of use of OCs.

Large epidemiological studies show no carcinogenic effect of oral contraceptives

Teratogenesis: There is no evidence for OCs being mutagenic or teratogenic or that they cause virilisation at contraceptive doses. There is no specific congenital abnormality associated with pill use either during or prior to pregnancy, and sex ratio and abortion rates are unaffected.

Acne: Diane is successful in the treatment of severe nodular acne, seborrhoea and mild cases of hirsuitism, and is also a reliable contraceptive with good cycle control and tolerance. Response is usually evident after 6-9 months. As this is a high-dose pill, patients should limit the duration of use to 2 years and then change to a triphasic pill or Marvelon. Marvelon (containing desogestrel) is less androgenic than levonorgestrol and in a recent study we found a marked, favourable effect in patients who had acne.

Neoplasia: There has always been concern about the possible carcinogenic effect of oral contraceptives. However, the results of large epidemiological studies are reassuring. OCs have a significantly protective effect against cancer of the *ovary* and *endometrium*. Clavel[1] reviewed 22 major epidemiological studies on OCs and *breast* cancer. The overall risk ratio was never found to increase compared to non-users. Several studies have shown an increased risk of developing cervical dysplasia or carcinoma of the

Breast examinations should be routine for all women, especially those on OCs

cervix amongst OC users or smokers or both. This increased risk has been linked to duration of use in excess of 5 years, but the casual association of the pill has not been confirmed because of the acknowledged difficulties in the studies, and the fact that pill users are more likely to have sexual behaviour patterns, which themselves are risk factors for cervical cancer, and women who had taken OCs were more likely to have had their cervical cancer diagnosed. The implications of these studies are uncertain because they are based on exposure to preparations that contained higher doses of estrogens and progestogens than are used today. Clearly, women who use OCs must have regular cervical cytology at yearly intervals, and women with abnormal cytology should be colposcoped. In addition, breast examination should be routine for women on OCs. *Hepatocellular carcinoma* is extremely rare. Forman[2] reported a higher risk of primary liver cancer among regular users compared with never-users of OCs, which increased with duration of use, but the incidence is exceptionally rare.

The substantial **beneficial effects** of OCs (including those of preventing unwanted pregnancies) far outweigh the rare risks. They prevent morbidity and mortality associated with pregnancy and childbirth, and reduce menstrual miseries (premenstrual tension, dysmenorrhoea, menorrhagia, irregular cycles), and in addition thousands of hospital admissions and surgical procedures are averted each year among pill users for conditions such as benign breast disease, ovarian cysts, ectopic pregnancy, endometriosis, pelvic inflammatory disease and anaemia.

OCs have a significantly protective effect against cancer of the ovaries and endometrium

The proven acceptability, efficacy, and safety of OCs and the benefits they infer, suggest that they will retain an important place in fertility control for the rest of this century at least. Once we realise that the main culprit is smoking and are convinced that low-dose pills are safe and effective, and that side-effects and risks are minimal, the rate of our own comfort and that of our patients will increase significantly.

Progestogen-only pills

Minipills occupy a small but significant place in contraceptive practice. Their use is limited because the risk of pregnancy is higher than with combined OCs (see Table 1) and they tend to disturb menstrual cycles. However, the minipill is extremely safe and is not associated with serious side effects of metabolic changes, or with any risk of morbidity or mortality.

Then minipill is particularly suitable for women over 45 and smokers over 35, or women who are intolerant of estrogen (lactation, hypertension). It relieves premenstrual tension significantly in some women. Contraceptive failures are mainly due to noncompliance, and meticulous attention must be paid to timing of pilltaking. The interval between pills should not be more than 27 hours and should preferably not immediately precede coitus, as the minipill depends on the altered cervical mucus for its anti-fertility effect, and this wanes at the end of the 24 hour period.

The main culprit is smoking

Therefore, if coitus usually takes place at night, the minipill should be taken in the morning. Bleeding disturbances do not usually cause problems provided patients are clearly advised beforehand. The proportion of *ectopic pregnancies* is increased, but the incidence is extremely low – much less than can be expected in women who use no contraceptives, as the pregnancy risk per se, is very small. There is no known association with neoplasia or coagulopathy or cardiovascular disease.

Part 3 to follow

Please note that *only* the tables in Part 1 of this article were previously published in *Contraception and Sexuality in Health and Disease* by K E Sapire, Johannesburg, McGraw-Hill Book Co. (SA), 1986.

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