FROM A COMMUNITY PHARMACIST

ORAL CONTRACEPTIVES

The most widely used type of oral contraceptives is the combined estrogen-progestogen product. Table 1 gives an indication of the range of combination products available today. The combination contraceptive products have a high efficacy resulting from 3 effects:-

1. the suppression of ovulation by estrogen and progesetagen;
2. the effect of the progestogen on the endometrium in such a way that it cannot readily support the nidation and growth of a fertilised ovum;
3. the thickening effect of the progestogen on the cervical mucus which prevents the sperm from passing through.

Progestogen	Dose	Oestrogen	Dose	Trade name
levonorgestrel	0.25mg	ethinylestradiol	0.03mg	Nordiol
levonorgestrel	0.15mg	ethinylestradiol	0.03mg	Nordette Microgynon
norgestrel	0.5mg	ethinylestradiol	0.05mg	Ovral
norethisterone	0.5mg	ethinylestradiol	0.03mg	Ovysmen
norethisterone	0.1mg	mestranol	0.05mg	Orthonovin
ethynodiol	1.0mg	mestranol	0.05mg	Ovulen 50

TABLE 1. Some combined estrogen-progestogen contraceptive products available locally

It has generally been regarded as essential that hormonal steroid contraceptives be available only on prescription, and that all women using them should be subjected to repeated intensive observation during their use. Suggestions have been made that medical intervention should only occur if the woman has a complaint. Paramedical personnel such as nurses, health visitors, midwives and pharmacists, have, in many countries been trained to provide oral contraception, but their use is still controversial, particularly in the developed western countries[1].

When commencing oral contraceptive therapy, it is advisable to start with a low dose estrogen formulation and to change to one with a higher estrogen formulation content should breakthrough bleeding occur.

SIDE EFFECTS

Beneficial side effects are: 1. a reduction in menstrual flow;
2. regularity of menstruation;
3. an almost invariable absence of dysmennorhea.

Minor side effects which do not constitute more than a minor nuisance to most patients are, fluid retention, nausea, exacerbation of variocosities, menorrhagia, and

breakthrough bleeding caused by the estrogen component. The progestogen component may cause acne, greasy hair, weight gain and breast fullness. The incidence of these symptoms may be reduced by switching to a different preparation with a lower ratio of the hormone thought to be responsible for the symptoms.

It should be noted that pregnancy is more likely to occur if there is breakthrough bleeding, so that if this persists, dosage should be promptly adjusted. The patient should be prescribed with a greater progestogen-estrogen ratio in the next cycle. Certain side-effects (eg. nausea, menstrual cramps, breast discomfort) are less common in overweight women and more so in the underweight; bodyweight should therefore be taken into consideration when prescribing on oral contraceptive.[2]

Serious side effects: Accumulated data shows that women who are on oral contraceptives are four times more likely than nonusers to suffer from myocardial infarction and three times more likely to have a fatal heart attack. The risk of venous thrombosis among users of low dose formulations is four times that of non-users; which risk increases to tenfold among users of high dose formulations.

Most studies have shown that all these risks skyrocket when oral contraceptives are used in conjunction with smoking, hypertension, high cholesterol, diabetes and/or advancing age.[3]

CONTRACEPTIVE FAILURE

Failure of contraception of combined preparations can occur due to:

1. failure to take the tablets daily;
2. another illness which interferes with the absorption of the hormones;
3. drug interactions.

1. As with any contraceptive method, the success of compliance is highly dependant on the motivation to prevent contraception. Should a tablet be missed, it can be taken within the next 12 hours. If, however, more than 12 hours have elapsed, the therapeutic effect in that cycle may be reduced. The other tablets should be taken at the usual time, but an addtiional contraceptive method should be used.

2. Vomiting and diarrhoea may interfere with absorption of the pill and reduce its contraceptive effect. In the event of such an upset, the pills for that cycle should be taken as usual but the use of an additional contraceptive method should be advised.

3. Oral contraceptives have a potential to inhibit the metabolism of other drugs. More importantly, several drugs significantly accelerate the biotransformation of oral contraceptives, by induction of liver enzymes, hence predisposing to loss of effectiveness and unplanned pregnancy. In clinical practice, such accellerated biotransformation may be suspected if breakthrough bleeding occurs, and the oral contraceptive dose increased or another contraceptive method used.

Estrogens undergo enterohepatic circultion. The estrogen conjugate excreted in the bile, enters the gastrointestinal tract where it is acted upon by bacteria in the gut releasing the active steroid for reabsorption. If the bacterial flora of the gut is suppressed by the use of an antibiotic, the steroid conjugates fail to undergo reabsorption resulting in a much more rapid clearance of the steroid from the body and inadequate suppression of the normal menstrual cycle.[1] [4]

TABLE 2. Drug interactions with contraceptives [2] [4] [5]

Class of drugs	Effect of Interaction
Antiinfective agents:	
Ampicillin, Rifampicin, Chloramphenicol, Tetracycline, Sulphonamides	Possible decrease in contraceptive reliability. Isolated cases of pregnancy reported
Hypoglycaemics:	
Insulin, oral hypoglycaemics	Control of diabetes may be altered
Barbiturates	Possible decrease in contraceptive reliabiltiy.
Antidepressants: Tricyclic antidepressants	Possibility of breakthrough bleeding and reduced contraceptive effect.
Anti inflammatory agents: Phenylbutazone, oxyphenbutazone	Possible decrease in contraceptive reliability.

EFFECT ON LACTATION

Women who are lactating sometimes find that the amount of milk is reduced by the use of some estrogen containing contraceptives. Low dose estrogen combination products and progestogen only preparations do not significantly effect the milk production. The amount of steroid injested by the breast fed infant is small and is readily metabolised.

(1) Avery G.S. — Drug Treatment — Principles and Practice of Clinical Pharmacology and Therapeutics.

(2) The Schering Oral Contraceptive Guide for Pharmacists and Nurses.

(3) Polmer F. — American Pharmacy Vol. NS21 No. 6 June 1981.

(4) Stockley I.H. — Pharmaceutical Journal November 6, 1982.

(5) Stockley I.H. — Drug Interaction Alert 4 (Boehringer Ingelheim).

RESEARCH

POTENTIAL MALE CONTRACEPTIVES

Gossypol

Investigations are currently being carried out into the use of gossypol as a male contraceptive.

Gossypol is a yellowish phenolic compound found in the seeds, leaves and roots of the cotton plant. Its contraceptive effects were not recognised until the 1950's, when a group of Chinese villagers became ill after cooking with cold-pressed cottonseed oil instead of the usual oil prepared through boiling. The cold pressed oil contained active gossypol which when taken in large amounts produces the symptoms of "cottonseed poisoning".

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There is little doubt about the effectiveness of gossypol as a contraceptive, but, because of the seriousness of poisoning, alot of studies are needed before it can be available for contraceptive uses. The results are so far encouraging in that it seems to cause no histological changes in body organs, no changes in libido, and sex hormone levels, and little changes in the testes.

Synthetic analogue — LHRH^A

Another candidate for male contraception is a synthetic analogue of leutenising hormone (LHRH). It has been reported that, LHRH^A significantly reduced the sperm counts of 8 men who participated in the study. However, 5 of the men developed temporary impotence during the administration of LHRH^A.

Futher tests are being conducted in an attempt to determine whether a fine-tuning of dosage levels will permit testosterone production to continue, yet block the production of sperm. Also, some tests are currently being carried out in which volunteers are given testosterone as well as LHRH^A in an attempt to determine if an outside supply of the steroid can counteract the LHRH^A induced decrease in steroid production, thus leaving the subject potent yet sterile.