Recent developments in oral contraceptives

With continuing improvements in oral hormonal contraception, Claire McNicholas outlines recent developments and current best practice

**ORAL FORMS OF HORMONAL CONTRACEPTION** include the combined oral contraceptive pill (COC), progestogen only pills (POP) and oral emergency contraception. Over the last number of years there have been significant improvements in dosage levels and side effect profiles.

**Combined oral contraceptives**

The COC has been in use now for over 35 years as a contraceptive. It combines oestrogen and progestogen in varying doses. Oestrogen prevents ovulation and progestogen alters cervical mucus thus causing endometrial change, which might interfere with implantation if fertilisation had occurred. Provided the COC is taken correctly, the efficacy is greater than 99%, with a failure rate of less than one per 100 women years. However, this success is dependent on correct usage, and some studies have shown a failure rate of 16% with incorrect use, particularly in the younger age group, with poor education and poor motivation. The majority of failures are due to incorrect use by the user.

Over the years the dosage of oestrogen in the pills has dropped dramatically. Initially 100µg was prescribed, now COCs normally contain 20µg or 30µg of oestrogen. With the lowering of the dose, non-smokers can now safely use the COC up to the age of the menopause, provided they have not used the COC for a cumulative 20 years. The cut off age for smokers is 35 years or earlier if the patient has reached a total of 15 pill taking years.

The progestogen used in the COC has changed over the years. Each different generation has achieved a considerable reduction in the total dose of steroid, with an associated decrease in androgenic and haemostatic side effects, without loss of contraceptive efficacy.

Before prescribing a COC, a careful history must include a risk factor history and advice should be given regarding risks and benefits. Women must be advised of the risk of venothromboembolism. Experts advise that second, as opposed to third, generation pills should be prescribed for women under the age of 30 who are free of risk factors for arterial disease. The side-effects of COCs can be divided into androgenic side-effects and progestogenic side-effects, as outlined by the Table.

Contraindications to COCs include heavy smokers over 35, women with breast cancer, liver abnormalities, focal migraine, a history of or risk factors for stroke or heart disease, diabetes with kidney, eye or other complications related to blood vessel damage, undiagnosed vaginal bleeding and finally risk factors for blood clotting.

Currently in MIMS there are 15 COCs available. A number of these may no longer be available in the near future, including Brevinor, Microgynon 30 and Ovranette. The majority of these are monophasic pills, providing a fixed dose of oestrogen and progestogen throughout the cycle. This fixed dose may cause greater endometrial hyperplasia and because of this some women develop dysmenorrhea on monophasic pills.

There are four triphasic pills available. Here we have three distinct phases where the dose of progestogen, and at times oestrogen, varies. Triphasic pills were designed to mimic normal cyclical hormonal changes. The low dose of progestogen at the start of the cycle, the rise in progestogen and oestrogen mid-cycle maintains the uterine lining with less chance of breakthrough bleeding. Finally the higher level of progestogen at the end of the cycle allows for more regular withdrawal bleeding.

Dianette combines oestrogen with an anti-androgen cyproterone. It is particularly useful for women with severe acne vulgaris but is also as effective as other COCs.

**Prescribing guidelines**

Efficacy depends on correct usage. COCs are started on the first day of menses and are immediately effective. They are taken once a day, preferably at a set time; however, there is a 12 hour window for a forgotten pill and provided the pill is taken within this window, efficacy is unchanged. If a pill is missed over these 12 hours then the advice is to finish out the pack as usual but take precautions for seven days. Equally, if a pill is vomited up within two hours of taking it, or a woman has severe diarrhoea, she must take precautions for the next seven days.

Broad spectrum antibiotics interfere with the absorption of the pill and women taking these antibiotics whilst on the pill should take precautions during the taking of the antibiotics and for seven days after the antibiotics finish. Patients on long-term antibiotics for acne should take extra precautions for the initial four weeks of therapy. Thereafter the intestinal flora involved in oestrogen absorption develop resistance and no extra precautions are needed.

Other drug interactions causing problems with COCs are hepatic enzyme inducers which increase the metabolism of hormonal contraceptives. These drugs include rifampicin, griseofulvin, spironolactone and all anti-epileptics (excluding sodium valproate and clonazepam). In these situations higher doses of hormonal contraceptive are required and a shorter pill-free interval in some cases. Of note, mega doses
Combined oral contraceptive pills – benefits and side effects

Benefits
The modern low dose COC has a protective effect against:

- Ovarian and endometrial cancer
- Ectopic pregnancy
- Menorrhagia
- Functional ovarian cysts
- Iron deficiency anaemia
- Dysmenorrhoea
- Uterine fibroids
- Benign breast disease

Side effects
Oestrogenic problems:
- Nausea
- Dizziness
- Premenstrual tension
- Irritability
- Cyclical weight gain
- Bloating
- Vaginal discharge
- Breast pain

Progestogenic problems:
- Dryness of the vagina
- Acne/oily skin
- Hirsutism
- Weight gain
- Depression
- Loss of libido
- Breast symptoms

Note: In these cases oestrogen dominant COCs may be prescribed, mindful that these may be associated with an increased risk of VT. Dianette may be helpful for those with acne problems.

Benefits of COC

- One to five years of pill use reduces the risk of ovarian cancer by 40%. This protection persists for at least 10 years after stopping the COC.
- The risk of endometrial cancer is reduced by 50% and this effect lasts for more than 10 years after stopping the COC. This benefit is thought to be due to suppression of ovulation and of normal menstruation.
- Protection against ectopic pregnancy because COC prevents ovulation.
- Reduction in blood loss and thus decreased anaemia.
- Decreased functional cysts.
- Less dysmenorrhoea because of less bleeding.
- Reduced uterine fibroids by 50%-70%
- Reduced benign breast disease by 50%-70%
- Decrease of 50% in incidence of pelvic inflammatory disease.
- The main problem with POP is irregular bleeding and in some women prolonged spells of amenorrhoea. Some women complain of breast tenderness which is often transient but may recur. Equally, ovarian cysts may occur because of the variable effects of POP on the ovary, thus a woman with a previous history of ovarian cysts might not consider use of POP.

Emergency contraception (EC)

In Ireland the rate of pregnancy terminations has doubled in the past 10-20 years. There were 6,400 official terminations amongst Irish women in the UK in 2000. Until recently the Yuzpe method (combined oestrogen and progestogen) was the only available form of emergency contraception. This is no longer available in Ireland, however a progestogen only product (Levonelle) was granted a product licence by the Irish Medical Board in May 2003.

Emergency contraception is designed for occasional use after unprotected coitus. It is not a substitute for regular contraceptive use and is less effective than a regular hormonal contraceptive. High dose progestogen with minimal side-effects, it is 98% effective if taken within 24 hours but can be taken up to 72 hours after unprotected sex.

Levonorgestrel is taken as 750µg x 2 tablets, the first as soon as possible but within 72 hours of unprotected sexual intercourse. The second tablet to be taken 12 hours later. It is thought that levonorgestrel may work at a number of levels – prevention of ovulation, altering tubal transport of sperm/ova, it may also alter the endometrial wall. Indications for use include unprotected sexual intercourse, potential barrier failure, potential pill failure or missed pill.

There are few contra-indications but these include – sensitivity to LNG or its constituents, and pregnancy. It must not be taken if unprotected sexual intercourse occurred more than 72 hours at the time of request. The date of last period must be noted. Side effects are minimal but 23% may suffer from nausea, 16.9% may have fatigue, 11.2% dizziness and 5.6% may have vomiting. Efficacy is 85% over 72 hours but it is more effective if taken in the first 24 hours. Return of menses is early in 15%, within two days of expected date in 57%, three to seven days beyond expected in 15% and over seven days beyond expected date in 13%. If return of menses is more than 10 days after the expected date then a pregnancy test should be done.

Claire McNicholas is in practice in Dublin