Giving advice on long-acting contraception

Recent headlines have claimed that women are not being offered enough choice in terms of contraception. In addition to the many brands of oral contraceptive pill, there are numerous other types of contraceptives for women, from implants to vaginal rings. In the first of two articles on contraception, Sarah Pillai looks at the long-acting contraceptives available.

For most women, contraception amounts to a lifestyle choice. I write “women” advisedly. Men can use condoms or withdrawal methods but vasectomy, which is irreversible in most instances, provides the only reliable long-term method for them. Although male hormonal methods of contraception have been researched for some years and have been found to be effective and relatively low in side effects, the challenge to the pharmaceutical industry to get people to perceive this as an acceptable option is considerable. So, back to women. All women are different and no single method is suitable for all. Contraception should take into account many factors, such as the stage in a woman’s life, the potential (and need) for future fertility, risk of sexually transmitted infections, menstrual patterns, acceptability of bleeding patterns and cultural influences (consider the two case studies on this page.)

The days of “the pill” as a first-line method of contraception are gone and there is a trend towards offering long-acting reversible contraception (LARC; i.e., where the contraceptive needs to be administered less than once per month and is reversible). There are National Institute for Health and Clinical Excellence guidelines (see Resources) relating to the use of these contraceptives and the increasing use of these methods is being promoted by the Government. These methods are: intrauterine contraceptive device (IUCD), intrauterine system (IUS), injectable progestogen and subdermal progestogenic implant. Such methods should not be overlooked. They provide safe and highly effective contraception as well as offering non-contraceptive benefits, such as treatment of menorrhagia. Moreover, NICE suggests financial benefits even after only one year of use compared with short-acting contraception.

Basic mechanisms
Contraceptives can be defined by their mechanism of action, for example, those that work by providing a barrier to sperm. To understand fully how other types of contraceptives work, readers might like to remind themselves of the stages of the menstrual cycle (see Panel 1, p390). The cycle is regulated via the hypothamalo-pituitary axis and other mechanisms.

The most effective methods of contraception prevent ovulation as their primary action. Both oestrogen and progestogen reduce the production of follicle stimulating hormone (FSH) and luteinising hormone (LH), meaning that the ovaries are not stimulated and there is no LH surge.

Progestogen also makes cervical mucus hostile to sperm and has an effect on the tubular motility of cilia in the Fallopian tubes, and so these act as secondary mechanisms should ovulation occur.

It should be noted that the effect of progestogen-containing contraceptives on ovulation may be affected by factors such as the type and strength of progestogen and with older progestogen-only pills.

Case studies

Case 1: Jenna is 16 years old and started using Implanon six months ago. She has vaginal bleeding most days, which is light but annoying. She has recently changed her partner and experiences pain during intercourse and postcoital bleeding.

Case 2: Lucy, aged 24 years, is taking Microgynon but she regularly forgets to take it and wants a more reliable method. She does not want to start a family for at least five years because she is still in full-time education.

Suggested actions are on p392
Injectable progestogens DMPA (depot medroxyprogesterone acetate; DMPA) and Noristerat (norethisterone enantate) are injectable progestogen-only contraceptives. Noristerat is rarely used because it has a licence for short-term use only (eg, according to the British National Formulary, the injection may be repeated once) and its injection interval is only eight weeks. Depo-Provera, given as an intramuscular injection into the buttock or upper arm, has been in use in the UK since 1984 and use can be continued for years. It has a licence for 12 weeks but, in practice, an injection is effective for at least two weeks after this.

DM PA induces amenorrhoea in most women (70 per cent by 12 months) so can be useful for women with problems relating to the menstrual cycle, such as migraines, menstrual epilepsy and menorrhagia. However, it is not licensed for this indication. On the other hand, some women find amenorrhoea unacceptable, so patients must be made aware of this possibility.

As with other progestogen-only methods of contraception, DMPA can have a prolonged effect in that, in some women, normal fertility may not return for up to a year after use. This is true even after one injection, so it is not suitable if a pregnancy is desired within a year of stopping contraception. There is no evidence of long-term loss of fertility.

As with all progestogen-only methods of contraception, irregular vaginal bleeding can be problematic (see Panel 2). There is no evidence to suggest that reducing the injection interval will help normalise bleeding patterns, although some practitioners try this.

Because DMPA reduces the levels of circulating oestriadiol in most women, there is a theoretical risk of reduction of bone mineral density (BMD). A reduction in BMD has been seen in a few studies but this returns to normal after the DMPA is stopped. Nevertheless, there are been concerns about the use of DMPA in adolescents (who will be laying down bone mass) and Committee on Safety of Medicines guidelines suggest caution in this group. However, providing the risks are discussed and other risk factors for osteoporosis are assessed (eg, family history of osteoporosis, heavy smoking, poor diet and sedentary lifestyle) the benefits generally outweigh the disadvantages.

Similarly, although an increased fracture risk with DMPA has not been demonstrated it may be logical to discuss stopping this contraceptive with women over 45 years. Such women are nearing the menopause so it is predicted that bone mass will

Panel 1: Menstrual cycle

**Follicular phase** From menses to ovulation, oestradiol levels rise in response to follicle stimulating hormone from the pituitary gland. This stimulates the follicle on the ovary to mature until ovulation.

**Ovulation** The ovum is released from the surface of the ovary at around day 14 of a normal 28 day cycle in response to a surge of luteinising hormone.

**Luteal phase** The ruptured follicle forms a corpus luteum producing progesterone, which stimulates the endometrial lining to proliferate in readiness for the blastocyst to implant. If implantation does not occur, the endometrial lining is shed in menstruation, which generally lasts four to seven days. The process then starts again.

Panel 2: Vaginal bleeding as a side effect of progestogen-only contraceptives

Undesirable vaginal bleeding patterns, ranging from amenorrhoea to frequent prolonged bleeding, can be a feature of any progestogen-only contraceptive. The unopposed progestogen makes the endometrium fragile and this can break down from time to time. However, dysfunctional bleeding must be investigated if it occurs after the first three months of use — sexually transmitted infections (STIs), such as chlamydia and gonorrhoea, can cause bleeding, particularly after intercourse, as can pregnancy. Risk factors should be considered and other symptoms sought, such as painful or difficult sexual intercourse, postcoital bleeding, pelvic pain, heavy bleeding or abnormal discharge, which might indicate an underlying cause. Tests should be done to eliminate STIs and pregnancy. Cervical screening history should also be established, and screening undertaken if appropriate. Drug interactions and compliance should also be assessed.

If the bleeding has been investigated, and the likely cause is the progestogen-only contraceptive, options can be discussed. The bleeding pattern may vary between methods and individuals, so if a woman experiences problems with one method, another progestogen-only method can still be tried.

With progestogen-only pills, there is no evidence that switching to another or taking two pills each day will help, but either may be tried.

With progestogenic long-acting reversible contraceptive methods, non-steroidal anti-inflammatory drugs (NSAIDs), oestrogen or doxycycline may help settle the bleeding (unlicensed indications). For further reading on this subject, there is a guideline written by the Clinical Effectiveness Unit of the Faculty of Sexual and Reproductive Health, which sets out the evidence available (see Further reading).

For example, when women using a progestogen-only injectable contraceptive with unscheduled bleeding, mefenamic acid 300mg bd for five days can reduce the length of a bleeding episode but has little effect on bleeding in the longer term. For women with light or heavy bleeding with a progestogen-only implant, oestrogen or doxycycline may help settle the bleeding. However, the dosing regimen and duration of use are not specified. In trials investigating the effect of doxycycline on endometrial bleeding, doses such as 20mg bd have been used.

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Panel 3: Advantages and disadvantages of long-acting reversible contraception

<table>
<thead>
<tr>
<th>Method</th>
<th>Depo-Provera</th>
<th>Subdermal implant</th>
<th>IUS</th>
<th>IUCD</th>
<th>Female sterilisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfect use failure rate</td>
<td>&lt; 0.4% over two years</td>
<td>0.01% over three years</td>
<td>&lt; 1% over five years</td>
<td>&lt; 2% over five years</td>
<td>0.05%</td>
</tr>
<tr>
<td>Advantages</td>
<td>Long-acting; amenorrhoea rates high; excellent method for non-compliance with pill taking; user friendly</td>
<td>No user failure; immediately reversible; lasts for three years</td>
<td>Non contraceptive benefits (see main text)</td>
<td>Non hormonal; can be used as emergency contraception; lasts for 10 years</td>
<td>Once only intervention</td>
</tr>
<tr>
<td>Disadvantages</td>
<td>May have delayed effect on fertility after stopping; sometimes causes nuisance bleeding; amenorrhoea may be unacceptable; concerns about affects on bone density</td>
<td>Nuisance bleeding in some; deep implant removals difficult; needs specialist training for fitting and removal</td>
<td>Nuisance bleeding in some; amenorrhoea sometimes unacceptable; risks of procedure include pelvic inflammatory disease and perforation; needs specialist for fitting and removal</td>
<td>Can increase menorrhagia; Irreversible; anaesthetic risks of insertion include pelvic inflammatory pregnancy</td>
<td></td>
</tr>
</tbody>
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Dysfunctional bleeding must be investigated if it occurs after the first three months of use of a progestogen-only contraceptive.

Start to fall and coming off the DMPA may allow bone density to recover before this.

In summary, it is advised that:

- In women aged under 18 years DMPA may be used as first-line contraception after all options have been discussed and if other options are considered unsuitable or unacceptable.
- A re-evaluation of the risks and benefits of treatment for all women should be carried out every two years in those who wish to continue use.
- For women with significant lifestyle or medical risk factors for osteoporosis, other methods of contraception should be considered.

Implants

The popularity of implants appears to be increasing. Many women ask to try implants because they know they have had a successful experience with them. The implant is particularly suitable for women in whom other methods are unsuitable, and who are prepared to tolerate minor side effects for the advantage of high protection. Young people are often targeted to try this method, but it may also be advantageous for older women who have trouble-some menses, or who are on DMPA and nearing the menopause because this method does not appear to have the same effect on BM D.

The only implant licensed in the UK is Implanon, which is a single rod device releasing etonogestrel. It contains 68mg of etonogestrel dispersed in a membrane of ethylene vinyl acetate, and each implant can be used for three years. Its main effect is to prevent ovulation, but it also has progestogenic activity on the cervical mucus and endometrium. The progestogen levels achieved are steady, and just above the level needed to prevent ovulation — so not as high as levels achieved with Depo-Provera.

Implanon is probably the most effective of all reversible contraceptives but there is no effect on potential fertility once the implant is removed. However, of all the progestogenic methods, this product has the highest rate of unacceptable bleeding, and women must be counselled fully before they are prescribed it. The implant can also produce amenorrhoea, and as already mentioned, counselling is required.

Implanon was originally thought to have no interaction with enzyme inducers, but cases of failure with HAART have been reported and caution is advised. The recommendation is now to use alternative contraception while taking an enzyme inducer and for four weeks afterwards.

The implant is inserted subcutaneously in the inner side of the non-dominant upper arm, 8–10cm above the elbow. It needs to be removed after use, either when the three years have elapsed or sooner if the woman requests. Some site reactions take place, including scarring and bruising, and the client must be warned of these.

Insertion (and removal) should be done by a healthcare professional with appropriate training. Use of an anaesthetic spray or lidocaine 1% per cent is recommended. If implants are inserted too deeply problems include neural or vascular damage and migration of the implant, which makes removal difficult.

Intrauterine system

The IUS Mirena slowly releases levonorgestrel into the endometrial cavity. The circulating levels of progestogen are, therefore, lower than those achieved with injections, implants or pills. The system is effective for five years as a contraceptive but it is also licensed for treatment of menorrhagia and as an adjunct to hormone replacement therapy to protect the endometrium.

As the systemic levels of levonorgestrel are low, the main effects occur within the endometrium and cervical mucus, as described above for progestogen methods. There is some effect on ovulation in a few cycles but generally, ovulation is maintained. There
is no long-term effect on fertility once the device is removed.

The contraceptive efficacy of this method is high, and its ability to decrease menorrhagia and protect the endometrium makes it popular among both women and gynaecologists. Most women will have a reduction of 90 per cent of bleeding within a year of use, around 20 per cent become amenorrhoeic and many more experience oligomenorrhoea. Mirena is used as an alternative to sterilisation in many women because its efficacy is similar but future fertility is maintained and, being less invasive, the procedure has lower risks. It is contraindicated in women with unexplained vaginal bleeding, as well as women who have other disorders of the uterus, such as anatomical abnormalities, trophoblastic disease or fibroids distorting the uterine cavity. The progestogen content also makes current breast cancer a contraindication. Mirena does not interact with enzyme inducers and, contrary to common misconception, it is not contraindicated in nulliparous women.

U nwanted effects include perforation of the uterine cavity (one per 500 insertions), expulsion of the device, pelvic inflammatory disease after the fitting and functional ovarian cysts (although these are generally of little significance). The rate of ectopic pregnancy is approximately 5 per cent of all failures (which is around one per 300 women years). In the past, a history of ectopic pregnancy was a contraindication for any intrauterine method, but with such low rates this is no longer the case. Fitting should occur normally within the first seven days of the menstrual cycle to ensure immediate protection. However, the system may be inserted at any time if there is no possibility of pregnancy, but seven days, additional precautions should be taken in this case. It can also be inserted four weeks after giving birth.

Non-hormonal LARC
IUCDs and female sterilisation are non-hormonal methods of LARC.

Intrauterine contraceptive device The IUCD (or copper coil) releases copper ions within the uterine cavity. Because these are toxic to sperm and ova, fertilisation rarely occurs. The presence of the IUCD within the uterine cavity also prevents implantation, and it is this effect that makes it useful as an emergency contraceptive fitted before implantation of a fertilised egg (licensed for up to five days after the earliest predicted day of ovulation).

The efficacy is high, although slightly less than with Mirena. Banded T devices, such as the T-Safe Cu380S, are the first choice of device because they have a lower pregnancy rate than devices without copper sleeves. The maximum licensed duration of use is 10 years for the T-Safe Cu380S. Other IUCDs, such as Multiload and NovaT, have a shorter licence because of the slightly higher failure rates with this type of non-banded device. However, any copper device may be retained until the menopause if fitted after the user is 40 years old.

Complications include perforation, expulsion and pelvic infection, as with the IUS. There is also usually increased menstrual blood loss — around 30 per cent heavier than the normal for an individual — and menstruation can also be prolonged.

Contraindications are the same as those for Mirena, apart from breast cancer. Again, nulliparity is not a contraindication.

IUCDs are particularly suitable for women who do not wish to use a hormonal method of contraception. They can be fitted at any time in the menstrual cycle, providing there is no reasonable likelihood that the woman is pregnant. For the purposes of emergency contraception, an IUCD may be fitted up to day 19 of a 28-day cycle. IUCDs may also be fitted four weeks after giving birth.

Sterilisation Sterilisation is outside the scope of this article but should be considered in a contraceptive consultation. Male sterilisation is around 10 times more effective than female, and has fewer complications at surgery. Sterilisation should always be seen as irreversible even though reversals have been successful in both men and women. It is usually not considered on the NHS unless LARC methods have been offered and declined. Some surgeons limit the operation to couples who are over the age of 35 years.

Conclusion The long-acting reversible methods of contraception offer choice for women who want a highly effective, non-user-dependent method. Healthcare professionals have traditionally offered the short-acting contraceptives, such as the oral contraceptive pill or condoms as first-line contraception for almost everyone. It is now time for us all to offer a full range of contraception so that each woman can make an informed choice. Panel 3 (p391) compares the methods discussed in this article.

Short-acting contraceptive methods will be covered in the next CPD article, to be published on 24 October 2009.

CPD articles are commissioned by The Journal and are not peer reviewed.

Suggestions for case studies on p389

Case 1 This patient needs to be checked for STIs, particularly chlamydia, and examined to exclude pelvic inflammatory disease as well as other causes for her bleeding. If this is all normal, a trial of a combined oral contraceptive pill for three months, taken continuously, may settle her bleeding (if she does not have any contraindications for use).

Case 2 Depo-Provera would be an option for this patient. If she has taken the pill consistently for seven days she will be covered contraceptively straight away. If not, she will need to use alternative contraception for seven days after the injection.

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www.pjonline.com

References

Further reading
http://guidance.nice.org.uk.
www.ffprhc.org.uk

Resources

Faculty of Sexual and Reproductive Healthcare Clinical Guidance. "Management of unscheduled bleeding in women using hormonal contraception" is available at www.ffprhc.org.uk.

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