The members' enquiry service: frequently asked questions September 2001–August 2002 and an illustrative CEU response

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Background

The new Clinical Effectiveness Unit (CEU) for the Faculty of Family Planning and Reproductive Health Care (FFPRHC) was established in September 2002.[1] As part of its work programme, the Unit provides evidence-based responses to clinical enquiries submitted by Faculty members. In developing our approach to researching and answering members' enquiries, we have reviewed the topic areas of questions received by the Faculty's former clinical effectiveness team during the last 12 months of its work. In this article, we present an overview of enquiry topics received between September 2001 and August 2002. As an illustrative example of our approach to members' enquiries, we also include our response to one frequently asked question, namely the impact of long-term depot medroxyprogesterone acetate (DMPA) on bone mineral density (BMD). Further illustrative responses, relating to commonly asked questions, will be provided in future issues of the *Journal of Family Planning and Reproductive Health Care*.

From September 2001 to August 2002, the former clinical effectiveness team handled 347 queries from Faculty members. These were received mainly by telephone, with a minority by e-mail or letter. The topic areas of these enquiries are summarised in Figure 1.

The commonest topic area (73 enquiries) concerned the use of intrauterine devices (IUDs). Enquiries covered standards for IUD insertion including antimicrobial prophylaxis and screening for sexually transmitted infections. Almost equally popular were questions about the use of the combined oral contraceptive pill (COC), contraindications to its use, and drug interactions. Several Faculty members enquired which hormonal contraceptive would be most suitable for a patient with a given clinical condition or co-morbidity. Members also asked about progestogen-only methods of contraception (POCs): their effects on BMD, dose and timing, and drug interactions.

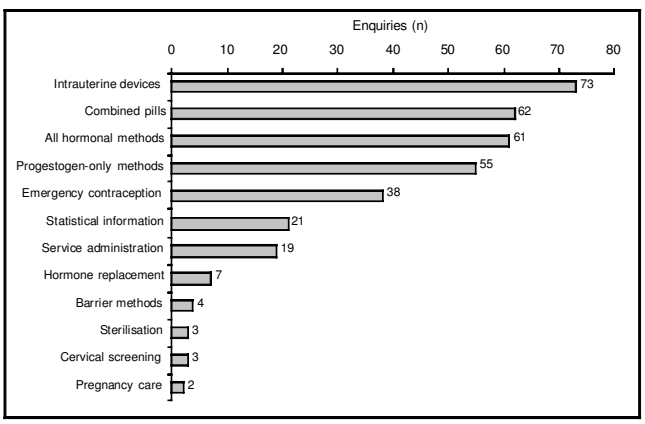

Figure 1 *Topic areas of members' enquiries between September 2001 and August 2002*

Concerning oral emergency contraception, queries related to efficacy, dose and timing, drug interactions, advance provision, and provision by nurses, pharmacists and in schools. The former team also answered requests for varied statistics and information on audit standards. Members also sought advice on record keeping, patient waiting times, staff-to-patient ratios, and emergency protocols.

Only a few Faculty members asked about the use of hormone replacement therapy, barrier methods of contraception, sterilisation, or cervical screening.

Table 1 summarises the themes of the 10 most common topic areas addressed in members' enquiries over the 12-month period. The illustrative response included in this article addresses the first theme. Themes 2 and 3 will be addressed in illustrative responses to be included in the next two issues of this journal.

To date, the new CEU has prepared evidence-based responses to almost 100 members' enquiries. Mechanisms are currently being developed whereby members' questions and CEU responses will be posted on the Faculty website. We hope to include a 'search facility' so that other members can determine if their own query has already been answered by the Unit.

Table 1 *The 10 most common themes of members' enquiries between September 2001 and August 2002*

1	Long-term use of DMPA (Depo-Provera) and its effects on oestrogen levels and bone mineral density.
2	Recommendations for sexually transmitted infection screening and antibiotic prophylaxis at intrauterine device (IUD) insertion.
3	Double-dosing of the progestogen-only pill (POP) for women > 70 kg in weight.
4	Management of asymptomatic patients with an IUD *in situ* and actinomyces-like organisms (ALOs) found on a cervical smear.
5	Provision of emergency, and routine contraception, by nurses.
6	Management of late DMPA (Depo-Provera) injections.
7	Use of contraceptive steroids by women with a personal or family history of cardiovascular disease and/or risk factors for cardiovascular disease.
8	Use of contraceptive steroids by women with hereditary or acquired disorders.
9	Efficacy, dose and timing of progestogen-only emergency contraception (POEC).
10	Drug interactions with the combined oral contraceptive pill (COC).

Illustrative CEU response

Clinical question

For women using long-term DMPA or Depo-Provera, who have low oestradiol levels, what management is necessary to prevent adverse effects on BMD?

Summary of response

There is no consensus as to whether there is a relationship between serum oestradiol levels and BMD and, if so, what threshold of serum oestradiol would indicate referral for bone densitometry. One recent study has suggested a threshold level of 52 pmol/l as necessitating referral, however this study suffered from methodological problems. A 2002 Faculty Aid to Continuing Professional Development (CPD) Topics (FACT) has stated that routine measurement of serum oestradiol levels in women using DMPA is unjustified. However, women with known risk factors for low BMD who have chosen DMPA contraception can be referred for bone densitometry screening. If the BMD is low, these women can be advised to choose an alternative method of contraception. The FACT does not recommend the administration of exogenous oestrogen.

The CEU does not recommend serum oestradiol measurement in the management of women with risk factors for low BMD who are on long-term DMPA but, where indicated, such women can be referred for bone densitometry.

Evidence-based medicine question (which guided our literature search strategy)

Population: Women with long-term Depo-Provera use and low oestradiol levels.
Intervention: Treatment for low oestradiol levels.
Outcome: Effects on BMD.

Information sources

The CEU searched the sources listed in Table 2 in developing this Member's Enquiry Response.

Most of the concerns about long-term use of Depo-Provera relate to its hypo-oestrogenic effects and any possible consequences for BMD. Osteopenia has been defined by the World Health Organization (WHO) as between –1 and –2.5 standard deviations of the mean value of peak bone mass in young normal women, while osteoporosis is defined as a BMD with a T-score less than –2.5.

Evidence reviewed

Existing FFPRHC and Royal College of Obstetricians and Gynaecologists (RCOG) guidance. A FACT[2] on Depo-Provera and bone density mentions that cross-sectional studies have shown that serum oestradiol levels in users may range from 15 to 318 pmol/l,[3–6] and that after up to 5 years of use most women have serum oestradiol levels above those of postmenopausal women. Additionally, these serum oestradiol levels are found to be in the early follicular phase range for women who ovulate. Therefore, DMPA users are not usually oestrogen-deficient. In addition, the FACT mentions two studies that have shown that there is no significant correlation between bone density and serum oestradiol levels.[5,6] The recommendations made by the FACT are:

- All women who are considering the use of DMPA should be told that studies have found an association between long-term DMPA use and loss of bone mass.
- Women should be encouraged to build up, or maintain, their bone mass through attention to diet and exercise while those with risk factors for low BMD, such as smokers or those on long-term high-dose corticosteroid therapy, should be discouraged from using this contraceptive method.
- This contraceptive method is known to cause low serum oestradiol levels. Therefore routine measurement of serum oestradiol is unjustified, but women who have additional risk factors for low BMD, such as smokers or perimenopausal women, can be referred for bone densitometry. If there is concern about osteopenia and risk of fracture after some years of use, the bone density should be checked. However, the threshold for triggering this investigation remains undetermined.
- The author did not feel that there was an evidence base for the administration of exogenous oestrogen.

WHO publications. The use of Depo-Provera by women in the 18–45-year-old age group is classified as Category 1 by WHO (unrestricted use).[7] The use of Depo-Provera by women under 18, and over 45, years of age is classified as Category 2, which means that the benefits of using the contraceptive usually outweigh any theoretical risks. The publication also mentions that for these latter groups there are theoretical concerns regarding the hypo-oestrogenic effects of DMPA use.

MEDLINE and EMBASE from 1996 to 2002. A 2002 study published in the *Journal of Family Planning and Reproductive Health Care* investigated DMPA-related bone loss in a general practice setting.[8] This study did, however, use a very small number of participants and therefore the results are questionable. A cohort of women aged 15–49 years were offered DMPA for a 5-year period with other methods as a first-line contraceptive.[8] All patients had serum oestradiol measured and those with levels < 52 pmol/l underwent bone densitometry. Based on this study, the authors concluded that 75% of those who use DMPA for 2 years or longer will have very low oestradiol levels (< 52 pmol/l) and about 50% of these will have spinal osteopenia or osteoporosis. The practical implications included an acknowledgement that the cause of low BMD is unclear and there is uncertainty about recovering lost BMD after stopping DMPA. The authors advised that DMPA use without bone densitometry should be avoided in women with risk factors for osteoporosis. Additionally, women who have used DMPA for 5 years should discuss hypo-oestrogenism with their doctor. Pre-injection oestradiol levels may be determined if the woman does not wish to stop DMPA and levels < 52 pmol/l might reasonably indicate bone densitometry.[8]

One review by the author of the FACT above looked at three studies, which focused on the issue of BMD and use of Depo-Provera in adolescents.[9] This mentions that no

Table 2 *Sources used in developing the Member's Enquiry Response*

Source searched	Information identified
Existing FFPRHC and RCOG guidance	See text
National Guidelines Clearing House	No relevant information
WHO publications: *Improving access to quality care in family planning: medical eligibility criteria for contraceptive use* (2000) and *Selected practice recommendations for contraceptive use* (2002)	See text
The Cochrane Library	No relevant information
MEDLINE and EMBASE from 1996 to 2002	See text
PRODIGY guidance on amenorrhoea	See text

FFPRHC, Faculty of Family Planning and Reproductive Health Care; RCOG, Royal College of Obstetricians and Gynaecologists; WHO, World Health Organization.

published studies have shown a linear relationship between oestradiol levels and BMD in teenagers. It recommends that serum oestradiol levels and BMD [by dual-energy X-ray absorptiometry (DEXA) scan] should be determined after 3 to 5 years of using Depo-Provera. Depending on the results of the DEXA scan, the teenager can then be advised on an appropriate method of contraception.[9]

PRODIGY guidance on amenorrhoea. This guidance[10] states that there is no consensus on the need for BMD measurements, oestrogen status or the use of 'add-back' oestrogen and other measures for long-term DMPA users. It further mentions that there are some recommendations that long-term users with risk factors for osteoporosis or oestrogen deficiency should have their serum oestradiol levels measured with referral for bone densitometry. The manufacturers of Depo-Provera recommend that women reaching the menopause after long-term DMPA use should consider HRT.[11]

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