



## Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit

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### MEMBERS' ENQUIRY RESPONSE

Enquiry Reference: 2478

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#### A: Question

What is the significance of a raised Follicle-Stimulating Hormone (FSH) level (FSH=15.1 iu/l) in a 22 year old woman with Systemic Lupus Erythematosus (SLE) who has been on Depot Medroxyprogesterone Acetate (DMPA), has been amenorrhoeic for 1 year and complains of flushes?

#### B: Response

In women using DMPA amenorrhoea is more likely with increased duration of use. 30-35% of women are amenorrhoeic after 3 months and 70.3% amenorrhoeic by 12 months. It would therefore not be unusual to experience amenorrhoea after 12 months of DMPA use. With DMPA use there is a potential delay in return to full fertility but no evidence of permanent infertility.

Autoimmune conditions have been cited as a possible cause of premature menopause and there is some evidence to suggest that individuals with SLE are more likely to experience menstrual irregularities than "healthy" women, including amenorrhoea and premature menopause. It is recommended that when testing for ovulation failure FSH levels are tested on more than two occasions at least one or two months apart as FSH levels can vary on a daily basis if a person is perimenopausal. FSH levels which would be strongly suggestive of premature menopause would be >30iu/l.

Individuals with SLE will often experience night sweats and therefore this symptom may be related to SLE rather than menopause.

The CEU would advise that whilst elevated, the levels of FSH are not high enough to confirm premature ovarian failure (POF). From the clinical information provided and a single FSH measurement it is impossible to tell whether the slightly elevated FSH is due to reduced ovarian reserve, the inhibitory effect of DMPA on ovarian activity or (if the last injection was more than 12 weeks ago) return of ovulation.

Given that there is some evidence to suggest that women with SLE may be at increased risk of premature menopause, if the clinician or patient is concerned the woman could be offered an alternative method of contraception which would not mask menstrual bleeding, delay the return of fertility or interfere with gonadotrophin levels. If amenorrhoea persists FSH levels can then be monitored on several occasions 1 or 2 months apart.

#### C: Evidence-Based Medicine Question (which guided our literature search strategy)

*Population:* Women with Systemic Lupus Erythematosus

*Intervention:* DMPA

*Outcome:* Significance of elevated follicle-stimulating hormone levels and hot flushes

**Keywords:** Systemic Lupus Erythematosus, Lupus, DMPA, FSH, menopause, 2478

## D: Information Sources

The CEU searched the following sources in developing this Member's Enquiry Response

Source Searched	Information Identified
Existing FSRH and RCOG guidance	See below
The National Guidelines Clearing House	No relevant information
The United Kingdom Medical Eligibility Criteria for Contraceptive Use (2005/2006) The United Kingdom Selected Practice Recommendations for Contraceptive Use (2002) The World Health Organization Medical Eligibility Criteria for Contraceptive Use (2004) The World Health Organization Selected Practice Recommendations for Contraceptive Use (2005)	No relevant information
The Cochrane Library	No relevant information
MEDLINE and EMBASE from 1996 to 2008	See below

## E: Evidence Reviewed

DMPA works primarily by inhibiting ovulation<sup>(1-3)</sup>. There is a thickening of the cervical mucus inhibiting sperm penetration into the reproductive tract and in addition changes to the endometrium make it an unfavourable environment for implantation<sup>(3)</sup>.

Bleeding changes are common in women using DMPA. Amenorrhoea with DMPA is more likely with increased duration of use<sup>(4)</sup> and 30-35% of women are amenorrhoeic after 3 months with 70.3% by 12 months<sup>(5)</sup>. It would therefore not be unusual to experience amenorrhoea after 12 months of DMPA use. With DMPA use there is a potential delay in return to full fertility but no evidence of permanent infertility.

High levels of FSH are uncommon during the reproductive years and could be indicative of early menopause. It is recommended that when testing for ovulation failure FSH levels are tested on more than two occasions at least one or two months apart as FSH levels can vary on a daily basis if a person is perimenopausal or menopausal<sup>(6)</sup>.

Autoimmune conditions have been cited as a possible cause of premature menopause and there is some evidence to suggest that individuals with SLE are more likely to experience menstrual irregularities than "healthy" women including amenorrhoea and premature menopause<sup>(7;8)</sup>. However FSH levels which would be suggestive of ovarian failure in conjunction with amenorrhoea would be those >30iu/l. In this individual the FSH levels are currently not within the range expected for someone experiencing early menopause.

The CEU would suggest that whilst elevated, the levels of FSH are not currently within the range that would be indicative of premature ovarian failure (POF). Whilst hot flushes are a known menopausal symptom, individuals with SLE will often experience night sweats and therefore this symptom may be related to SLE rather than elevated FSH. However given that there is some evidence to suggest that women with SLE may be more likely to experience menstrual irregularities including premature menopause, it might be beneficial to change to a method which does not mask bleeding or delay the return of fertility. If amenorrhoea persists FSH levels can then be monitored on several occasions 1 or 2 months apart.

## F: References

- (1) Pharmacia Limited. Depo-Provera 150mg/ml Injection. <http://www.medicines.org.uk>. 2007.
- (2) Bhathena RK. The long-acting progestogen-only contraceptive injections: an update. British Journal of Obstetrics and Gynaecology 2001;108:3-8.

- (3) Faculty of Sexual and Reproductive Health Care. Progestogen-only injectables (In Press). 2007.
- (4) Task Force on Long-Acting Systemic Agents for Fertility Regulation Special Programme of Research DaRTiHR. A multicentred phase III comparative clinical trial of depot-medroxyprogesterone acetate given three-monthly at doses of 100mg or 150mg: II. The comparison of bleeding patterns. *Contraception* 1987;35(6):591-610.
- (5) Canto De Cetina TE, Canto P, Luna MO. Effect of counselling to improve compliance in Mexican women receiving depot-medroxyprogesterone acetate. *Contraception* 2001;63:143-6.
- (6) Faculty of Family Planning and Reproductive Healthcare Clinical Effectiveness Unit. Contraception for Women Aged over 40 Years. *Journal of Family Planning and Reproductive Health Care* 2005;31(1):51-64.
- (7) Medeiros MMC, Silveira VAL, Menezes APT, Carvalho RC. Risk factors for ovarian failure in patients with systemic lupus erthematosus. *Brazilian Journal of Medical and Biological Research* 2001;34:1561-8.
- (8) Fatnoon NNA, Azarisman SMS, Zainal D. Prevalence and risk factors for menstrual disorders among systemic lupus erthematosus patients. *Singaore Medical Journal* 2008;49(5):413-8.

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Enquiry response by JC