# All Wales Clinical Biochemistry Audit Group

# Biochemical Investigation of Menopausal Status and Monitoring of Hormone Replacement Therapy (HRT)

## Introduction

A survey of methods and responses to requests for the biochemical investigation of menopausal status and monitoring of hormone replacement therapy (HRT) in Wales was presented at an audit meeting in October 1997. The survey showed variations in practice and a need for guidelines. The following recommendations are made in the light of discussions at audit group meetings, published reviews and consultation with colleagues.

## 1. Methodologies

(i) All laboratories should provide or have access to:

a range of reproductive hormones assays; and

advice on appropriate tests and interpretation of results.

(ii) Reference ranges for the same method groups should be the same. If there is insufficient data to establish reference ranges, the manufacturer's ranges should be used.

(iii) The turn-round time for all requests should not exceed 1 week, except for assisted fertilisation where there is a need for same day results.

## 2. Investigation of Menopausal Status

The average age at menopause is between 49 and 51 years, with the transition starting at a median age of 44 years (range 34-55) [1]. The most important guide to clinical decision-making is a careful clinical history [2]. Hormonal assays have little place in the diagnosis, except in younger patients (age < 45 years) suspected to have a premature menopause. The most characteristic hormonal feature reported for irregular cycles is the finding of a clearly elevated FSH. However, FSH levels during the menopausal transition are variable and elevated levels can return to normal [1, 2, 3, 4]. Oestradiol measurement is of little additional value [3]. It is recommended that:

(i) Patients should be tested when amenorrhoeic or in the follicular phase of the cycle, with the day of the cycle stated on the request form.

(ii) **Women ≥ 45 years old**: measure **FSH only**, but only if there is clinical doubt about menopausal status. If the FSH is not clearly elevated (i.e. below upper limit of the mid-cycle reference range) and there remains clinical uncertainty about menopausal status, the test can be repeated at intervals of 6 months. Measure oestradiol **only** if there is post-menopausal bleeding (and the patient is not on HRT).

(iii) **Women < 45 years old** (suspected to have a premature menopause): measure FSH, LH and oestradiol (while off oral contraception or HRT), with other investigations as appropriate (e.g. prolactin, testosterone, cortisol, ovarian antibodies), depending on the clinical findings. Pregnancy needs to be excluded. In women who have had a hysterectomy without an oophorectomy, measure FSH only, but only if the patient becomes symptomatic.

## 3. Monitoring of Hormone Replacement Therapy (HRT)

(i) Before initiating treatment, measure FSH and oestradiol to increase the diagnostic certainty of menopausal transition if the woman is not clearly menopausal.

(ii) **Implants**: In order to avoid tachyphylaxis, measure oestradiol approximately 3 weeks before appointment at the implant clinic, so that the result is available when the patient attends for repeat implant. Adjust the dose of implant according to the following table:

| Oestradiol concentration (pmol/l): | <250 | 250-749 | 750-1000 | >1000 |
|---|---|---|---|---|
| Recommended implant dosage: | 100 mg | 50 mg | 25 mg | Nil |

Oestradiol values may vary according to the assay.

(iii) **Patches**: Measure oestradiol **only** if it is necessary to test for non-absorption.

(iv) **Oral**: Measure oestradiol **only** if it is necessary to test for non-compliance. Due to the mixture of oestrogens in oral preparations (which have differing cross-reactivities in immunoassays), reported oestradiol concentrations may be inaccurate, making it difficult to interpret the results. Please consult a local gynaecologist concerning problems with specific oral preparations. If it is felt that any biochemical monitoring is required in addition to clinical monitoring, FSH measurements would also be appropriate.

(v) "Target" ranges for oestradiol are poorly defined [5-10] and as with all drugs, concentrations will depend on the interval between the time of the sample and the time of the last dose.

## 4. Acceptance of Requests

Samples should be retained for at least 1 week if tests requested by a clinician are not initially analysed by laboratories following these recommendations. A comment should be added to reports when tests are not done stating that: "These tests are not routinely considered appropriate in the investigation of menopausal status or monitoring of HRT (as appropriate). Further guidance is available from the laboratory; samples have been retained for 1 week." Requests for specific investigations should be accepted where there is supporting clinical information on the request form.

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## References

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