SUBFERTILITY-BIOCHEMICAL ASSESSMENT AND INITIAL INVESTIGATIONS

SUBFERTILITY

- Subfertility is defined as failure to conceive after 2 years. Appropriate investigations can begin after 1 year.
- The basic guidelines below are designed to allow initial classification of problems (typically in primary care) and appropriate specialist referral for further investigation.
- Where possible, suggested cut-offs mirror those used in current laboratory reporting comments.

FEMALES

NB: **Women with fertility problems are no more likely to have thyroid disease than the general population. Thyroid function testing should thus be confined to women with symptoms of thyroid disease (NICE CG156)**

Women who are concerned about their fertility should not be offered a blood test to measure prolactin. This test should only be offered to women who have an ovulatory disorder, galactorrhoea or a pituitary tumour.

A pre-requisite for logical investigation is knowledge of the frequency and regularity of menstrual cycles.

REGULAR MENSTRUAL CYCLE

Measure mid-luteal phase progesterone (e.g day 21 of 28 day cycle; day 28 of 35 day cycle): Sample should be taken 7 days before the expected period and interpreted when the next period has begun.

- ≥30 nmol/L is consistent with ovulation and no further biochemical assessment is indicated
- <30 nmol/L (confirmed) requires further investigation as below for anovulation/oligo-ovulation

IRREGULAR MENSTRUAL CYCLE

Measure LH and FSH (days 3-5)
Progesterone should be measured. Depending on the timing of the menstrual period, this may need to be conducted every 3rd or 4th day from day 21, or later in the cycle (for example day 28 of a 35 day cycle) and repeated weekly thereafter until the next menstrual cycle starts.

ANOVULATION AND OLIGO-OVULATION

Measure FSH, and testosterone (in early follicular phase days 2-7, if cycle history allows).

NB. Progesterone measurement has no role in the assessment of subfertility in females without a menstrual cycle.

Significant patterns include:

- FSH > 27 IU/L indicates primary ovarian failure on more than one occasion. In women <40 year increased FSH suggestive of premature ovarian insufficiency. Recommend confirm by repeat FSH in 4-6 weeks as per NICE guidance NG23. Consider specialist referral if confirmed.
- FSH & LH <1.5 IU/L suggests possible pituitary or hypothalamic disease. Anorexia and the effect of other medication should also be considered.
- Mildly raised testosterone (>3.5 nmol/L) suggests possible polycystic ovary syndrome in the absence of interfering drugs.
- A confirmed testosterone > 5 nmol/L requires further investigation: Consider 17- hydroxy progesterone (17-OHP), dehydroepiandrosterone sulphate (DHEAS) and androstenedione measurement

MALES

The key initial investigation is semen analysis performed according to a recommended protocol.

NORMAL SEMEN ANALYSIS

No further biochemical assessment required

AZOOSPERMIA OR OLIGOZOOSPERMIA

Measure FSH, LH and testosterone (ideally early AM (8 – 10 am), fasting sample)

Significant patterns include:

- Elevated FSH (>12 U/L)/LH (>9 U/L) suggests primary gonadal failure
- Reduced FSH (<1.5 U/L)/LH (<1.5 U/L) plus low testosterone (typically <8 nmol/L) suggests hypothalamic or pituitary disease

REFERENCES

1. Clinical Review – ABC of Subfertility. *BMJ* 2003; 327

2. ACP Best practice No 170, J Clin Pathol 2003;56:261-267

3. Fertility problems: assessment and treatment. Clinical guideline [CG156] Published date: February 2013 Last updated: September 2017

4. Menopause: diagnosis and management (NG 23)