

## Assessment and treatment for people with fertility problems:

NICE guideline

### INTRODUCTION

The National Institute of Health and Care Excellence (NICE) has published an updated clinical guideline on assessment and treatment for people with fertility problems.<sup>1</sup> The guideline covers the pathway from advice and information for people concerned about fertility to assisted reproduction techniques.

The guideline includes recommendations on medical and surgical management of male factor fertility problems, classification and treatment of ovulatory disorders, management of endometriosis, tubal and ovarian surgery, donor insemination, oocyte donation, and procedures during in vitro fertilisation (IVF). This summary will concentrate on initial advice and assessment and criteria for IVF treatment.

### GUIDANCE

#### Initial advice

The guideline includes useful tables and figures which provide information about cumulative pregnancy rates (Table 1), and the effect of maternal age on IVF success rates (Table 2). Over 80% of couples will conceive within 1 year if the woman is <40 years, they do not use contraception and have regular sexual intercourse. Of those who do not conceive in the first year, about half will do so in the second year. Sexual intercourse

every 2 to 3 days optimises the chance of pregnancy. A woman with regular menstrual cycles is likely to be ovulating.

There is no change to advice to inform women who are trying to become pregnant that no more than 1 or 2 units of alcohol once or twice per week and avoiding episodes of intoxication reduces the risk of harming a developing foetus. Excessive alcohol intake is detrimental to semen quality. Smoking is likely to reduce fertility in women and passive smoking is likely to affect the chance of conceiving. There is an association between smoking and reduced semen quality although the impact of this on male fertility is uncertain.

Women with a body mass index (BMI) of  $\geq 30$  take longer to conceive and weight loss increases the chances of conception if they are not ovulating. Group programmes involving exercise and dietary advice lead to more pregnancies than weight-loss advice alone. Men with a BMI of  $\geq 30$  are also likely to have reduced fertility.

The guideline reminds healthcare practitioners to advise women who are trying to get pregnant to take folic acid.

#### Initial assessment

The guidance recommends clinical assessment and investigation for a woman

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**Table 1. Cumulative probability of conceiving a clinical pregnancy by the number of menstrual cycles**

Age category, years	Pregnant after 1 year (12 cycles), %	Pregnant after 2 years (24 cycles), %
19–26	92	98
27–29	87	95
30–34	86	94
35–39	82	90

*From NICE guideline 156. Cumulative probability of conceiving a clinical pregnancy by the number of menstrual cycles attempting to conceive in different age categories (assuming vaginal intercourse occurs twice per week) [Reproduced with permission: Dunson DB, Baird DD, Colombo B (2004). Increased infertility with age in men and women. *Obstetrics and Gynecology* 103: 51–6].*

**Table 2. Cumulative probability of conceiving a clinical pregnancy by the number of cycles of insemination**

Woman's age, years	ICI using thawed semen [Schwartz <i>et al</i> 1982] <sup>2</sup>		Woman's age, years	ICI using fresh semen (van Noord-Zaadstra <i>et al</i> , 1991) <sup>3</sup>		Woman's age, years	IUI using thawed semen (HFEA data and personal communication)	
	6 cycles	12 cycles		6 cycles	12 cycles		6 cycles	12 cycles
<30	50%	70%	<31	58%	76%	—	—	—
30–34	43%	62%	31–35	50%	71%	<35	63%	86%
>34	33%	54%	>35	39%	55%	35–39	50%	75%

ICI = intracervical insemination. IUI = intrauterine insemination. From NICE guideline 156.

### Box 1. WHO reference ranges for semen analysis tests

- **Semen volume:** ≥1.5 ml
- **pH:** ≥7.2
- **Sperm concentration:** ≥15 million spermatozoa per ml
- **Total sperm number:** ≥39 million spermatozoa per ejaculate
- **Total motility (percentage of progressive motility and non-progressive motility):** ≥40% motile or ≥32% with progressive motility
- **Vitality:** ≥58% live spermatozoa
- **Sperm morphology (percentage of normal forms):** ≥4%

### REFERENCES

1. National Institute for Health and Care Excellence. *Fertility: assessment and treatment for people with fertility problems*. CG156. London: NICE, 2013. <http://www.nice.org.uk/CG156> [accessed 18 Nov 2013].
2. Schwartz D, Mayaux MJ. Female fecundity as a function of age: results of artificial insemination in 2193 nulliparous women with azoospermic husbands. *Federation CECOS. N Engl J Med* 1982; **306**: 404–406.
3. Van Noord-Zaadstra BM, Looman CW, Alsbach H, *et al*. Delaying childbearing: effect of age on fecundity and outcome of pregnancy. *BMJ* 1991; **302**: 1361–1365.

### Provenance

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of reproductive age, who has not conceived after 1 year of unprotected vaginal sexual intercourse, in the absence of any known cause of infertility. It is suggested that couples should be seen together. Referral for counselling should be considered at all stages of investigation and/or treatment because of the impact of infertility and infertility treatment. An earlier referral for specialist consultation is appropriate when the woman is aged ≥36 years, there is a known cause of infertility, or a history of predisposing factors. People at risk of infertility because of planned treatment (for example, for cancer), should be offered referral to a fertility specialist.

The results of semen analysis should be compared with the World Health Organization reference values (Box 1). If the result of the first semen analysis is abnormal, a repeat confirmatory test should be undertaken 3 months later to allow time for the cycle of spermatozoa formation to be completed. If gross azoospermia or severe oligozoospermia has been detected the repeat test should be undertaken as soon as possible.

Ovulation should be confirmed with a blood test to measure serum progesterone in the mid-luteal phase (day 21 of a 28-day cycle). If cycles are irregular the test may need to be conducted later in the cycle (for example day 28 of a 35-day cycle) and repeated weekly thereafter until the next menstrual cycle starts. Women with irregular cycles should also have their gonadotropins measured. Basal body temperature does not reliably predict ovulation and is not recommended. Prolactin or thyroid function tests are not required but rubella status should be checked and women should be up to date with cervical screening.

A woman's age should be used as an initial predictor of her overall chance of success through natural conception. The guidance says there is no place for ovarian volume, ovarian blood flow, inhibin B or oestradiol (E2) as individual tests to predict

any outcome of fertility treatment. Testing for ovarian response to IVF should use total antral follicle count, anti-Müllerian hormone or FSH levels.

Oral ovarian stimulation agents (such as clomiphene citrate, anastrozole, or letrozole) should not be given to women with unexplained infertility.

### Further assessment and treatment

The guidance recommends IVF treatment for women with unexplained infertility who have not conceived after 2 years of regular unprotected sexual intercourse. Advice on the effect of lifestyle factors, age, BMI, and previous pregnancy on IVF treatment is included. Table 2 may be useful information for couples. Women <40 years who have not conceived after 2 years of regular unprotected intercourse or 12 cycles of artificial insemination (where ≥6 are by intrauterine insemination), should be offered 3 full cycles of IVF.

One full cycle of IVF should be offered if a woman is aged 40–42 years provided they have never previously had IVF treatment, there is no evidence of low ovarian reserve and there has been a discussion of the implications of IVF and pregnancy at this age. Any previous full IVF cycle, whether self- or NHS-funded, should count towards the total of 3 full cycles that should be offered by the NHS.

### Special circumstances

The guidance makes recommendations for management of couples where the man is HIV, hepatitis B, or hepatitis C-positive. Intrauterine insemination without ovarian stimulation can be considered as a treatment option for people who are unable or would find it very difficult, to have vaginal intercourse because of a physical disability or psychosexual problem, who are using partner or donor sperm, people with conditions that require specific consideration in relation to methods of conception (for example, after sperm washing where the man is HIV positive), and people in same-sex relationships.

### COMMENT

The NICE guideline provides useful information for healthcare professionals and patients. Local protocols for tests may differ. The expansion in eligibility for IVF treatment for older women has been welcomed but NICE guidance is based on clinical and cost-effectiveness concerns and commissioning organisations are likely to continue to vary in whether they consider the recommendations for IVF treatment affordable.