Infertility

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Definition

- **Definitions** of infertility vary, particularly with regard to length of time of regular, unprotected intercourse. Individual circumstances should be considered on their own merit, and couples should be seen when they think there is a problem.
- **Commonly used definitions** of infertility are 1 year or 2 years of involuntary failure to conceive, despite unprotected sexual intercourse.
- **Causes of infertility** may be idiopathic (30%), or secondary to ovulatory failure (27%), male factors (19%), tubal factors (14%) or endometriosis (5%).

Incidence

- **80 - 90% of all couples attempting to conceive are successful** after one year, rising to 95% after 2 years The monthly pregnancy rate is still 4-5% in couples with infertility up to 3 years (where the woman is approximately 30 years old)
- **The number of couples seeking help has increased** although it is suggested that there has been no major increase in prevalence, and theories such as a decline in sperm count due to environmental factors are controversial. Behavioral factors such as a tendency to delay childbearing may play a role.

History for both partners:

- Is essential to exclude possible causes of infertility and should include:
- Length of time since stopping contraception.
- Maternal age (fertility decreases with age)
- Details of cervical smear history, menstrual cycle, sexual history, drugs, occupation and previous surgery.
- Past history of mumps (in men) and sexually transmitted diseases (associated with tubal infertility) should be noted.

Examination

- **Female partner**: bimanual examination helps to exclude fibroids or other abdominal pathology.
- **Male partner**: Phimosis and balanitis as this may result in infected ejaculate leading to failure of in vitro fertilization. Examination of the testes may reveal lumps and undescended testes in some cases. Gynaecomastia should be noted. Exclude hernia, varicocoele and check testicular size.

Conditions which may present as infertility

- **Women:**
- **Ovarian cysts** - large cysts may be detected on bimanual examination.
- **Endometriosis** - patient may be tender on examination.
- **Polycystic ovarian syndrome** - often associated hirsuitism, acne and menstrual irregularity.
- **Hyperprolactinaemia** - may be associated with galactorrhoea and menstrual irregularity.
- **Anorexia nervosa** - patient is also normally amenorrhoeic
- **Hypothyroidism, pituitary tumor**
- **Drugs which increase incidence of luteinised unruptured ovarian follicles** include: non-steroidal anti-inflammatories.
- **Drugs associated with anovulation and ovarian failure** include: chemotherapeutic agents and cannabis.
- **Environmental factors** which may be affect fertility include: insecticides, herbicides and fungicides.

Conditions which may present as infertility

- **Men:**
- **Testicular tumour** - may be palpable on examination.
- **Maldescended testes** - absence of testes on examination.
- **Varicocele** - present in up to 25% of men seeking assessment for infertility.
- **Syndromes** - e.g. Klinefelter's syndrome, Immotile cilia syndrome.
- **Exposure to antispermatogeic agent** - e.g. drugs, irradiation, heat.
- **Hypogonadism**
- **Congenital absence of vas deferens** - 1-2% of infertile men.
- **Autoimmune** - e.g. post vasectomy
- **Drugs which may be associated with sperm or seminal abnormalities** include: sulphasalazine, nitrofurantoin, tetracycline, cimetidine, colchicine, allopurinol, some chemotherapeutic agents, cannabis, cocaine and anabolic steroids.
- **Drugs which may be associated with impotence or ejaculatory dysfunction** include: ketaconazole, alpha-blockers and propanolol.
- **Environmental factors** which may be affect fertility include: agricultural chemicals, x-ray exposure, solvents, and heavy metals.

Conditions which may present as infertility

- Both:
- Psychogenic factors
- Genital tract infection

Complications of infertility

- Psychiatric disorders may result from unintentional childlessness.
- Social and marital discord may occur.
- Complications may be secondary to the underlying cause.

Managemen

- **GENERAL ISSUES**
- **Local protocols should always be followed when managing the infertile couple.**
- It is important to involve both partners in all aspects of management. Discussion of wishes, plans, beliefs and motives are important.
- If the couple have not conceived within 3 years of stopping contraception, then the chance of spontaneous pregnancy in the next year is 25% or less.
- **Folate** supplements should be taken whilst trying to conceive and for the first 12 weeks of pregnancy in order to reduce the risk of neural tube defects.
- **Rubella status** should be checked. If seronegative, rubella vaccination is indicated and the woman should be advised not to become pregnant within one month of the vaccination.

Managemen

- **ADVICE**
- **Smoking** can affect fertility in men and maternal smoking in pregnancy can cause harm to the fetus, therefore both potential parents should be encouraged to stop.
- **Alcohol limitation** to 1 to 2 units once or twice a week (for the woman) is recommended. Excessive drinking in men can affect general and reproductive health and should therefore be discouraged.
- **Weight loss** should be encouraged in women with Body Mass Index greater than 30 as this is associated with a reduced pregnancy rate and poorer general health. There is no proven association between obesity in men and infertility, although obesity is associated with poorer general health.
- **Loose trousers** and underwear are recommended for men with poor quality sperm. They are also advised to avoid situations which may lead to testicular hyperthermia.
- **Timing of intercourse** using **temperature charts** and **luteinising hormone detection** methods has not been shown to improve fertility. Couples who seek advice on this issue should be encouraged to have regular sex (2 or 3 times a week) throughout the cycle.

Managemen

- **INITIAL INVESTIGATIONS**
- **Male partner:**
- Two fresh semen specimens should ideally be sent to the laboratory used by the infertility clinic
- Specimens sent 3 to 4 weeks apart will sample the same sperm population. Therefore if it is necessary to test a different sperm population, 12 weeks should elapse between specimens .
- **Female partner:**
- 9% of regular menstrual cycles may be anovulatory, therefore even women who have regular menstrual cycles ovulation should have ovulation confirmed by checking midluteal phase progesterone(day 22-24).
- Thyroid function and prolactin tests are of little value in women with a regular menstrual cycle, unless there are symptoms of thyroid disease or galactorrhoea.

REFERRAL CRITERIA

- **Decision to refer** should always be based on the individual couple's concerns and preferences.
- **Abnormality of any initial tests** suggests that secondary care involvement is required.
- **Deferment of referral** is acceptable if history, examination and investigations are normal in both partners, and the duration of infertility is less than 18 months.
- **Earlier referral may be prompted by factors including:**
  - **Maternal age** greater than 35 years: this is associated with a substantial decrease in the chance of success with in vitro fertilisation.
  - **Previous surgery** (female: abdo/pelvis, male: urogenital)
  - **Irregular menstrual cycle** (female)
  - **Previous sexually transmitted disease** (male and female) or pelvic inflammatory disease (female)
  - **Abnormal pelvic (female) or genital (male) examination**, varicocoele (male)

Management options in secondary care

- **In vitro fertilisation (IVF)**: This involves retrieval of the egg, which is mixed with sperm, incubated for 2-3 days, then the embryo is injected into the uterus via the cervix. It is a frequently used treatment for unexplained infertility and tubal disorders. The decision to treat depends on maternal age, previous pregnancy history and duration of infertility (criteria vary between health authorities). Spontaneous pregnancy may still occur at a rate of 4-5% in couples with infertility even up to 3 years, therefore in unexplained infertility waiting is an option often considered, taking into account maternal age. Pregnancy rates with IVF may range from 8% to 25% for each treatment cycle started (similar to the pregnancy rate in a fertile couple), depending greatly on centre factors and patient factors.

Management options in secondary care

- **Gamete intrafallopian transfer (GIFT)** is an alternative form of assisted conception which is effective in the management of unexplained infertility where the fallopian tubes are patent. This involves egg retrieval, mixing the eggs with the prepared sperm, then injecting the eggs with the sperm into the fallopian tube. However, IVF may be preferred because of the additional diagnostic information it provides and because it avoids laporoscopy and possibly general anaesthesia.

Management options in secondary care

- **Ovulation induction:** further investigation of ovulation disorders is usually necessary - this should only be carried out in a specialist infertility clinic - before ovulation induction may be considered. It is recommended that ovulation induction therapy is initiated in secondary or tertiary care . **Counselling**, with regard to the risks of multiple pregnancy, hyperovulation syndrome, fetal reduction and possible risk of ovarian cancer is given by secondary or tertiary care teams. **Clomiphene** is an anti-oestrogen which may be used in selected women as it is effective. Other treatments used include pulsatile gonatotrophin-releasing hormone and dopamine agonists (depending on cause of anovulation). Ovarian ultrasound monitoring is necessary when ovarian hyperstimulation treatments are being used. Ovarian stimulation with intra-uterine insemination may be effective in the management of subfertile women with mild endometriosis.

Management options in secondary care

- **Tubal surgery:** this may be appropriate, depending on the site and severity of the tubal disease.

- **Surgical ablation** of minimal or mild endometriosis improves fertility in subfertile women with endometriosis. **Danazol** and other medical treatments for endometriosis do not enhance fertility.

- **Male infertility:** Further investigations may include endocrine tests, microbiological semen analysis, imaging of the urogenital tract, testicular biopsy. Treatment options depend on the diagnosis and may include bromocriptine (only if there is hyperprolactinaemia), gonadotrophins, kinin enhancing drugs, intra-uterine insemination, intracytoplasmic sperm injection (injection of a single sperm into the inner cellular stucture of the egg), and surgery.