# Infertility

## What can a couple expect when trying to ?conceive

- Within a year of regular intercourse, 90% of fertile couples should become pregnant. After two years, this rises to 95%.
- λ Thus, 510% of normal fertile couples take more than a year or two to conceive.
- λ The usual criterion to define subfertility, and initiate investigations, is a delay of more than one year.

#### **Causes of infertility**

- λ Sperm defects or dysfunction30%
- λ Ovulation failure (e.g. PCOS)25%
- λ Tubal infective damage (chlamydia infection)

λ Unexplained infertility

λ Endometriosis (causing damage)5%

- λ Coital failure or infrequency5%
- λ Cervical mucus defects or dysfunction

3%

20%

25%

## Other factors affecting fertility

- λ Increasing age reduces a woman's fertility and the likelihood of successful treatment.
- Extremes of weight loss or obesity reduce female fertility.
- Smoking, particularly by women, reduces fertility.
- Longer duration of subfertility, particularly more than 3 years reduces fertility. A previous full term pregnancy is associated with a better chance of conception.

## ( Medical history (women

- λ Previous contraception and any problems (Such as "lost" IUCD)
- λ Previous pregnancies and outcome
- λ Medical history (Such as pelvic infection, Crohn's disease)
- λ Surgical history (Such as ovarian cyst, appendicectomy)
- λ Gynaecological history (Such as cone biopsy, cervical smear Hx)
- λ Current medical illness
- λ Drug treatments
- λ Diet

#### (Medical history (women

- λ Smoking, alcohol consumption, excessive caffeine intake
- λ Galactorrhoea
- λ Hirsutism
- λ Menstrual regularity and menorrhagia
- λ Dysmenorrhoea
- λ Intermenstrual or postcoital bleeding
- λ Preovulatory cervical mucus recognition
- λ Coital frequency and timing

## (Medical history (men

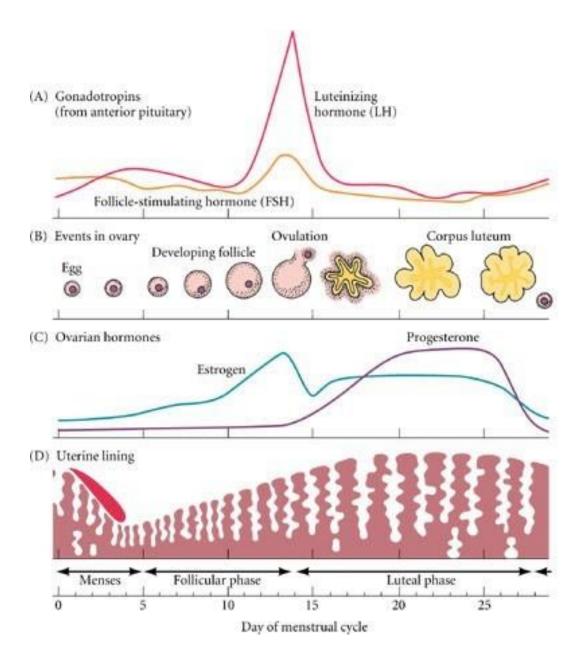
- λ Occupation (exposure to excessive heat or toxin)
- Medical history (such as mumps, venereal infections)
- λ Surgical history (such as orchidopexy, inguinal hernia repair)
- λ Current medical illness
- Prescribed drug treatments (such as sulfasalazine)
- λ Drug misuse (such as anabolic steroids)
- λ Smoking, alcohol consumption, excessive caffeine intake
- λ Erectile or ejaculatory difficulty

#### Physical examination

- $\lambda$  Examination of the woman should include:
  - Measurement of BMI
  - Assessment for any signs of endocrine disorder (e.g. PCOS)
  - Pelvic examination
- λ Examination of the man is not usually necessary unless indicated by:
  - -Medical history (such as previous orchidopexy, inguinal hernia repair, or testicular torsion)
  - -if initial semen analysis result is abnormal
- In most couples the initial history and examination will give no indication of the cause of their subfertility, and full investigations will be needed.

## (Investigations (sperm dysfunction

- Seminal analysis is the primary investigation for men with infertility.
- One poor analysis result is insufficient for making a diagnosis of sperm disorder. If the first result shows a low sperm count or complete absence of sperm, it should be repeated, preferably 2-3 months later.
- λ WHO criteria for normal semen analysis:
  - Volume >2.5 ml,
  - Sperm count >20 million/ml,
  - Motile >50%
  - Normal morphology >15%



## (Investigations (ovulation disorder

#### Midluteal progesterone level

- For women with irregular length cycles, mid-luteal progesterone level best measured at five day intervals from seven days before the earliest expected date of menstruation until the time they begin their next period.
- For women with regular cycles, mid-luteal progesterone level best measured 5-10 days before menstruation.
- λ Low mid-luteal progesterone level (generally <30 nmol/l) suggests anovulation or ovulatory dysfunction</p>

#### (Investigations (ovulation disorder

#### **FSH and LH levels**

- Levels of FSH and LH hormone should be measured between days two and five in women who have periods, or at random if cycles are infrequent or absent.
- λ Raised FSH indicates ovarian failure
- λ Raised LH (with normal FSH) suggests PCOS

#### **Prolactin**

- λ Hyperprolactinaemia is rare in the absence of amenorrhoea.
- λ if marginally raised with regular cycle may suggest PCOS; if raised with amenorrhoea suggests prolactinoma

#### (Investigations (ovulation disorder

#### Sex hormone binding globulin (SHBG(

SHBG would not routinely be investigated, but if there is uncertainty about a diagnosis of PCOS, a low SHBG provides supportive .evidence

#### (Investigations (fallopian tube damage

- Chlamydia serology is the best initial screen for tubal disorder. A raised chlamydia antibody titre ( > 1:256) is associated with a high likelihood of tubal damage.
- <sup>λ</sup> High antibody titres ( > 1:256) may indicate current or previous tubal infection, and both partners should be treated with an appropriate antibiotic (such as oxytetracycline, erythromycin, azithromycin, or ofloxacin).
- <sup>λ</sup> Treatment does not correct tubal damage but prevents reactivation if laparoscopy or other pelvic surgery is indicated.

#### (Management (Sperm dysfunction

Couples in which the man has sperm dysfunction need early referral for in vitro fertilisation, usually with intracytoplasmic sperm injection (the direct injection of a single sperm into each ). egg

#### Clomifene citrate

- Clomifene citrate is usually given on days 26 of the cycle
- The starting daily dose should not exceed 50 mg, and probably never 100 mg daily except in very obese women.
- Midluteal serum progesterone measurements can be used to check for an ovulatory response.
- Because of a possible association with later borderline ovarian tumours, clomifene should not be prescribed in nulliparous women for more than 12 months.

#### **Dopamine agonists**

- Dopamine agonists such as bromocriptine and cabergoline are safe and effective treatments for hyperprolactinaemia.
- However, the diagnosis and monitoring of women with presumed hyperprolactinaemia can be sufficiently complicated to warrant specialist referral.
- It is worth considering pharmacological causes for hyperprolactinaemia (such as dopamine antagonists, some antihypertensives, and major tranquillisers).
- λ It is unlikely that dopamine agonist treatment will overcome iatrogenic cause of raised prolactin levels.

#### **Metformin**

- Over 90% of women with oligomenorrhoea or amenorrhoea are reported to return to normal cycles with treatment, with 20% conceiving within six months.
- The starting dose of metformin is 500 mg daily. At this dose many women get more regular ovulatory cycles. If not the dose may be increased to 500 mg twice daily for a minimum of three months.
- If cycles become regular, it is worth continuing for six months at this dose. If a woman's cycle remains irregular the dose can be increased to 500 mg three times daily or 850 mg twice daily.

- Midluteal progesterone level 510 days before menstruation will indicate whether normal ovulation is occurring.
- Women still without periods or ovulatory progesterone levels can be given additional clomifene as described above.
- The combination of metformin and clomifene induces ovulation in about 90% of women with polycystic ovary syndrome.
- Metformin should be stopped when a woman has a +ve pregnancy test.

#### Management of fallopian tube damage

When positive chlamydia serology or HSG suggest fallopian tube damage, appropriate antibiotic treatment for chlamydia followed .by early referral for specialist opinion is indicated

## Indications for early referral to a specialist fertility clinic

- λ Woman's age > 38 years
- $\lambda$  Duration of infertility > 3 years
- λ Serum chlamydia antibody titre > 1:256
- λ FSH concentration in early follicular phase > 10 IU/I
- λ LH concentration in early follicular phase > 10 IU/I
- λ Abnormal seminal fluid analysis