Infertility

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Training Course in Sexual and Reproductive Health Research
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Infertility

- Definitions
- Influence of maternal and paternal age on fecundability
- Declining female fertility with age
- Prevalence of infertility
- Regional estimates of childlessness, primary infertility, and secondary infertility in developing countries
- General categories of infertility (WHO study)
- Distribution of infertility causes in developed countries
- Specific diagnoses of infertility, by developing status and region (WHO study)
- Infertility treatments and subsequent pregnancies
- Advice and information for the infertile couple
- Management of the infertile couple
- Evidence-based recommendations
Definitions

- **Infertility**: absence of conception after 12 months of regular, unprotected intercourse (commonly used medical definition of infertility). Inability to conceive within two years of exposure to pregnancy is the epidemiological definition recommended by the World Health Organization.

- **Primary infertility** means that the couple has never conceived, despite regular unprotected intercourse for a period of 12 months.

- **Secondary infertility** means that the couple has previously conceived, but is subsequently unable to conceive despite regular unprotected intercourse for a period of 12 months. If the woman has breastfed a previous infant, then exposure to pregnancy is calculated from the end of lactational amenorrhea.

- **Childlessness (demographic studies)**: inability to bear any children, either due to the inability to conceive or the inability to carry a pregnancy to a live birth. Childlessness at the end of the reproductive years is most effectively studied by using women in the oldest age cohort: women 45 to 49 years.

- **Infertility (demographic studies)**: inability of a non-contracepting sexually active woman to have a livebirth. Demographers have shifted the endpoint from conceptions to live births because it is difficult to collect complete data about conceptions in population-based studies. In addition, demographic analyses of infertility are often based on secondary data from demographic surveys that contain complete birth histories, but no information about induced abortions, miscarriages and stillbirths. It is common in demographic studies to use a period of exposure of five years.

- **Fecundability**: the probability of conception per menstrual cycle or monthly probability of conception for a sexually active couple not using birth control.
Influence of maternal and paternal age on fecundability

The observed proportion of planned pregnancies leading to birth conceived in ≤ 6 or in ≥ 12 months according to the father’s and the mother’s age

<table>
<thead>
<tr>
<th>Age groups</th>
<th>No. of couples</th>
<th>Percentage of couples conceiving within specified time interval (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Father’s age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 24</td>
<td>643</td>
<td>77.1</td>
</tr>
<tr>
<td>25-29</td>
<td>2692</td>
<td>78.4</td>
</tr>
<tr>
<td>30-34</td>
<td>2809</td>
<td>73.8</td>
</tr>
<tr>
<td>35-39</td>
<td>1153</td>
<td>68.6</td>
</tr>
<tr>
<td>≥ 40</td>
<td>573</td>
<td>66.3</td>
</tr>
<tr>
<td>Total n</td>
<td>7870</td>
<td></td>
</tr>
<tr>
<td>Mother’s age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 24</td>
<td>1625</td>
<td>76.4</td>
</tr>
<tr>
<td>25-29</td>
<td>3663</td>
<td>75.9</td>
</tr>
<tr>
<td>30-34</td>
<td>2466</td>
<td>73.8</td>
</tr>
<tr>
<td>35-39</td>
<td>680</td>
<td>62.8</td>
</tr>
<tr>
<td>≥ 40</td>
<td>81</td>
<td>59.3</td>
</tr>
<tr>
<td>Total n</td>
<td>8515</td>
<td></td>
</tr>
</tbody>
</table>

Declining female fertility with age

- Reduced quality of oocytes
- Ovulatory disorders
- Longer exposure to the risk of genital infections and iatrogenic infertility causes
- Increased uterine pathology
- Decreased frequency of intercourse
- Decreased partner's fertility
Prevalence of infertility (subfertility)

<table>
<thead>
<tr>
<th>Category of subfertility</th>
<th>Prevalence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unresolved primary subfertility in those women having or attempting to have at least one child</td>
<td>2.4-5.9</td>
</tr>
<tr>
<td>Resolved primary subfertility in those women having or attempting to have at least one child</td>
<td>10.0-12.1</td>
</tr>
<tr>
<td>Unresolved secondary subfertility in those women having or attempting to have more than one child</td>
<td>4.2-7.2</td>
</tr>
<tr>
<td>Resolved secondary subfertility in those women having or attempting to have more than one child</td>
<td>12.4</td>
</tr>
<tr>
<td>Any episode of primary subfertility in those women having or attempting to have at least one child</td>
<td>13.3</td>
</tr>
<tr>
<td>Any episode of secondary subfertility in those women having or attempting to have more than one child</td>
<td>17.4</td>
</tr>
<tr>
<td>Any episode of subfertility in those women having or attempting to have at least one child</td>
<td>20.7-32.6</td>
</tr>
</tbody>
</table>

Subfertility defined as failure to conceive after 12 months of regular unprotected intercourse or the occurrence of >2 consecutive miscarriages or stillbirths.

Infecundity, Infertility, and Childlessness in Developing Countries

Definitions

- **Childlessness**: Percentage of women who are currently married, have been so for at least five years, and who have no living children.
- **Primary infertility**: Percentage of women who have been married for the past five years, who have ever had sexual intercourse, who have not used contraception during the past five years, and who have not had any births.
- **Secondary infertility**: Percentage of women with no births in the past five years but who have had a birth at some time, among women who have been married for the past five years and did not use contraception during that period.
- **Secondary infecundity**: Percentage of women with no births and no pregnancies in the past five years but who have had a birth or pregnancy at some time, among women who have been married for the past five years but did not use contraception during that period.

This study utilizes data from 47 Demographic and Health Surveys in developing countries to examine levels, trends, and differentials in women’s inability to bear children. Overall, by age 45 to 49, only 3 percent of sexually experienced women have not had a birth. Countries with more than 5 percent of sexually experienced women age 45 to 49 without a birth include the Central African Republic, Cameroon, Mozambique, Niger, Haiti, Colombia, and Brazil.

Infecundity, Infertility, and Childlessness in Developing Countries

Middle and Eastern Africa have the highest average levels of secondary infecundity. These subregions are followed by Western Africa, Southern Africa, and South Asia, which have similar levels. The lowest levels of secondary infecundity are in South America.


OBJECTIVE: To determine if the decline in infertility has been uniform across subgroups.

DESIGN: Periodic data from the National Fertility Survey and the National Survey of Family Growth were used to determine which factors contributed to the decline in 12-month infertility in the United States. A woman is classified as “infertile” if she has not conceived a pregnancy after ≥12 months of unprotected intercourse with her husband or cohabiting partner.

SETTING: National Survey of Family Growth, a periodic US nationally representative study.

PATIENT(S): A nationally representative sample of married women aged 15-44 years, N = 15,303 for pooled data across 4 survey years.

MAIN OUTCOME MEASURE(S): Estimates of infertility prevalence among married women aged 15-44 years.

RESULT(S): The decline in 12-month infertility in the United States from 8.5% in 1982 and 7.4% in 2002 was significant. This decline was evident in nearly all subgroups of married women. In the multivariate analysis, 12-month infertility was more likely among women who were older and nulliparous, were non-Hispanic black or Hispanic, and did not have a college degree. The decline in 12-month infertility was observed even after controlling for the compositional differences of the population over time.

CONCLUSION(S): Among married women in the United States, there has been a significant decline in 12-month infertility, which cannot be explained by changes in the composition of the population from 1982-2002.


General categories of infertility, by developing status and region (WHO study)

<table>
<thead>
<tr>
<th>Categories</th>
<th>Developed countries</th>
<th>Africa</th>
<th>Asia</th>
<th>Latin America</th>
<th>East Mediterranean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Became pregnant</td>
<td>12</td>
<td>15</td>
<td>16</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>No cause found in both</td>
<td>14</td>
<td>5</td>
<td>13</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Female cause only</td>
<td>31</td>
<td>37</td>
<td>34</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Male cause only</td>
<td>22</td>
<td>8</td>
<td>13</td>
<td>22</td>
<td>19</td>
</tr>
<tr>
<td>Causes found in both</td>
<td>21</td>
<td>35</td>
<td>24</td>
<td>30</td>
<td>38</td>
</tr>
</tbody>
</table>

Distribution of infertility causes in developed countries

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Female cause only</td>
<td>35%</td>
<td>33%</td>
<td>50%</td>
</tr>
<tr>
<td>Male cause only</td>
<td>25%</td>
<td>20%</td>
<td>27%</td>
</tr>
<tr>
<td>Cause found in both</td>
<td>24%</td>
<td>39%</td>
<td>20%</td>
</tr>
<tr>
<td>No cause found in both</td>
<td>16%</td>
<td>8%</td>
<td>3%</td>
</tr>
</tbody>
</table>
Specific diagnoses of infertility, by developing status and region (WHO study)

<table>
<thead>
<tr>
<th>Categories</th>
<th>Developed</th>
<th>Africa</th>
<th>Asia</th>
<th>Latin America</th>
<th>East Mediterranean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No demonstrable cause</td>
<td>40</td>
<td>16</td>
<td>31</td>
<td>35</td>
<td>26</td>
</tr>
<tr>
<td>Bilateral tubal occlusion</td>
<td>11</td>
<td>49</td>
<td>14</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Pelvic adhesions</td>
<td>13</td>
<td>24</td>
<td>13</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Acquired tubal abnormality</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Anovulatory regular cycles</td>
<td>10</td>
<td>14</td>
<td>9</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Anovulatory oligomenorrhea</td>
<td>9</td>
<td>3</td>
<td>7</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>Ovulatory oligomenorrhea</td>
<td>7</td>
<td>4</td>
<td>11</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Hyperprolactinemia</td>
<td>7</td>
<td>5</td>
<td>7</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>6</td>
<td>1</td>
<td>10</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Male diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No demonstrable cause</td>
<td>49</td>
<td>46</td>
<td>58</td>
<td>41</td>
<td>28</td>
</tr>
</tbody>
</table>

Infertility treatments and subsequent pregnancies (N=444)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous pregnancies</td>
<td>99</td>
<td>22.3</td>
</tr>
<tr>
<td>Hormone treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>56</td>
<td>12.6</td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>1.1</td>
</tr>
<tr>
<td>Antibiotic treatment of the couple</td>
<td>42</td>
<td>9.5</td>
</tr>
<tr>
<td>Surgical treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>38</td>
<td>8.6</td>
</tr>
<tr>
<td>Male</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td>Artificial insemination with husband semen</td>
<td>58</td>
<td>13.1</td>
</tr>
<tr>
<td>Artificial insemination with donor semen</td>
<td>56</td>
<td>12.6</td>
</tr>
<tr>
<td>IVF or ICSI</td>
<td>80</td>
<td>18.0</td>
</tr>
<tr>
<td>Pregnancies after IVF or AIH failure</td>
<td>8</td>
<td>1.8</td>
</tr>
</tbody>
</table>
Advice and information for the infertile couple

- **Information about the chances of conceiving spontaneously** may be of great help to the couple. For couples who have been trying for less than a year, the success rate is between 80% and 90%. For couples who have been trying to conceive for up to 3 years, the success rate is about 40% in a 1-year period (equivalent to a monthly fecundity rate of 4-5%). For couples who have been trying for more than 3 years, the success rate is still up to 25% in a 1-year period. If a male or female subfertility factor has been identified, there is still a likelihood of spontaneous conception, although the success rates may be lower [NHS CRD, 1992; Himmel et al, 1997; Hargreave and Mills, 1998; Te Velde and Cohlen, 1999].

- **Assessment and investigations for infertility are not generally advised until the couple has been unable to achieve a pregnancy after a year of unprotected intercourse**. Some people who present with concerns about their fertility need only simple reassurance that the chance of conception is 84% in the first year if they do not use contraception and have regular sexual intercourse. About half of couples who do not conceive in the first year will conceive in the second year (a cumulative pregnancy rate of 92%) [National Collaborating Centre for Women’s and Children’s Health, 2004].

- **Regular sexual intercourse (two or three times a week) throughout the cycle** should ensure that intercourse falls within the fertile period. Timing of intercourse using temperature charts and luteinizing hormone detection methods causes stress and has not been shown to improve conception rates. They are therefore not recommended [Hargreave and Mills, 1998; National Collaborating Centre for Women’s and Children’s Health, 2004]. [Timing intercourse to conceive.]

- **Folic acid 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. Most women should take 400 micrograms daily. A higher dose of 5 mg daily is recommended for women who either have a family history of neural tube defect, who have had a baby with a neural tube defect, who are taking antiepileptic medication, or who have coeliac disease [Wald, 1991; Lumley et al, 2003; National Collaborating Centre for Women’s and Children’s Health, 2004].

- **Rubella** status should be checked. If seronegative, rubella vaccination is indicated and the woman should be advised not to become pregnant within 1 month of the vaccination [CMO, 2003].
Advice and information for the infertile couple

- **Smoking cessation is advisable for both men and women.** Smoking, including passive smoking has been shown to be detrimental to fertility in women [Hughes and Brennan, 1996; Augood et al, 1998; Hull et al, 2000; BMA, 2004]. In men, although there is no clear evidence that smoking delays conception or affects fertility, it may affect sperm quality and general health [BMA, 2004].

- **Alcohol limitation**
  - Women should be advised to limit alcohol to 1 to 2 units once or twice a week. The evidence for a link between alcohol and female infertility is conflicting, and the limits for safe consumption are not known, but until more is known, low consumption of alcohol when trying to become pregnant and during pregnancy is advisable [DH, 2003; National Collaborating Centre for Women's and Children's Health, 2004]. A unit of alcohol is about the same as a small glass (125 ml) of wine or a half-pint of beer.
  - Men should be informed that alcohol consumption within the Department of Health's recommendations of 3 to 4 units a day is unlikely to affect their fertility. Excessive alcohol consumption can be detrimental to semen quality [National Collaborating Centre for Women's and Children's Health, 2004].

- **Weight**
  - Weight loss should be encouraged in women with a body mass index (BMI) greater than 29, as this is likely to increase their chance of ovulation and therefore conception. There is no proven association between male obesity and infertility, although obesity is associated with poorer general health, a reduction in sperm motility and increased DNA fragmentation [Rich-Edwards et al, 2002; Kort et al, 2003a; Kort et al, 2003b; National Collaborating Centre for Women's and Children's Health, 2004].
  - Women who have a body mass index of less than 19 and either amenorrhoea or irregular menstruation should be advised that gaining weight is likely to increase their chance of conception [National Collaborating Centre for Women's and Children's Health, 2004].

- **Nutrition**
  - A well-balanced diet will contribute to general good health for both partners. Although there is little research on nutritional factors in infertility, there have been studies suggesting that nutritional deficiencies may play a role; e.g. vitamins C, D, E, selenium, zinc, and folate deficiencies may affect sperm quality [Wong et al, 2000].
  - There is no consistent evidence to link consumption of caffienated beverages (tea, coffee, and cola) and infertility [National Collaborating Centre for Women's and Children's Health, 2004].

- **Clothing.** Men should be informed that although there is an association between an elevated scrotal temperature and reduced semen quality, it is uncertain whether wearing loose-fitting underwear improves semen quality [Tiemessen et al, 1996; Munkelwitz and Gilbert, 1998; National Collaborating Centre for Women's and Children's Health, 2004].

*Infertility (Prodigy, UK)*
Management of the infertile couple
Management of the infertile couple

Evaluation of the infertile couple

Female partner
- History
- Physical examination
- Serologic tests
- Cervical cultures

Male partner
- History
- Physical examination
- Serologic tests

Direct the evaluation in particular direction

Next step
## Management of the infertile couple

### History of the female partner

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>General data, fertility history</td>
<td>Age; ethnic group; religion; occupation; duration of infertility; number and outcome of previous pregnancies; postpartum or abortion complications</td>
</tr>
<tr>
<td>Family history</td>
<td>Infertility; spontaneous abortion; stillbirths; genetic diseases; DES exposure in utero</td>
</tr>
<tr>
<td>General history</td>
<td>Diabetes; thyroid disease; adrenal disease; tuberculosis; autoimmune disease; other systemic diseases; iatrogenic factors</td>
</tr>
<tr>
<td>Gynecological history</td>
<td>Previous use of contraceptive methods; PID; STD; recurrent vaginitis, cervicitis or cystitis; iatrogenic factors</td>
</tr>
<tr>
<td>Menstrual history</td>
<td>Age at menarche; menstrual rhythm; duration and amount of bleeding; dysmenorrhea; premenstrual syndrome; abnormal bleeding</td>
</tr>
<tr>
<td>Symptoms and signs related to ovulatory disorders</td>
<td>Stress, psychologic factors; anorexia, weight loss, exercise; bulimia; overweight, obesity; anosmia; galactorrhea; hirsutism; hot flushes; cyclic pelvic pains</td>
</tr>
<tr>
<td>Habits</td>
<td>Occupational or environmental exposures; nutritional habits; sport; smoking; alcohol; drug consumption</td>
</tr>
<tr>
<td>Sexual history</td>
<td>Knowledge and use of the fertile period; frequency of vaginal intercourse; dyspareunia; orgasm</td>
</tr>
</tbody>
</table>
Management of the infertile couple

<table>
<thead>
<tr>
<th>History of the female partner - iatrogenic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypogonadotrophic hypogonadism</strong></td>
</tr>
<tr>
<td><strong>Hyperprolactinemia</strong></td>
</tr>
<tr>
<td><strong>Hypergonadotrophic hypogonadism</strong></td>
</tr>
<tr>
<td><strong>Tuboperitoneal factor</strong></td>
</tr>
<tr>
<td><strong>Uterine factor</strong></td>
</tr>
<tr>
<td><strong>Cervical factor</strong></td>
</tr>
</tbody>
</table>
Management of the infertile couple

<table>
<thead>
<tr>
<th>History of the male partner</th>
<th>Iatrogenic factors</th>
</tr>
</thead>
</table>

- **General data, fertility history**: Age; ethnic group; religion; occupation; previous marriages and their outcome; primary or secondary infertility; duration of infertility.
- **Family history**: Infertility; spontaneous abortion; stillbirths; genetic diseases.
- **General history**: Diabetes; adrenal disease; cystic fibrosis; tuberculosis; bronchiectasis; chronic infections; high fever (in the past 6 months); allergies; renal diseases; liver diseases; neurological diseases; drugs.
- **Urogenital history**: Cryptorchidism; precocious or delayed puberty; testicular injury; orchitis (mumps); history of STD; epididymitis; prostatitis; vesiculitis; urethritis; genital dermatosis.
- **Surgery relevant to infertility**: Orchiopexy; orchietomy; inguinal hernia operation; testicular detorsion; varicocelectomy; epididymovasostomy; vasovasostomy; vasectomy; prostatectomy; bladder operations; repair of hypospadias; circumcision.
- **Habits**: Occupational or environmental exposures; nutritional habits; sport; smoking; alcohol; drug consumption; sauna; tight pants.
- **Sexual history**: Knowledge and use of the fertile period; frequency of intercourse; libido; erection; dyspareunia; ejaculation; orgasm.
# Management of the infertile couple

## History of the male partner - iatrogenic factors, occupational and environmental exposures

<table>
<thead>
<tr>
<th>Condition</th>
<th>Exposure Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypogonadotrophic hypogonadism</td>
<td>Androgens; cyproterone; medroxyprogesterone acetate; pituitary operations; radiation of the head</td>
</tr>
<tr>
<td>Hyperprolactinemia</td>
<td>Amitriptyline, amphetamines, antidepressants, butyrophenones, cimetidine, estrogens, imipramine, methadone, methyldopa, metoclopramide, morphine, pimozide, phenothiazines, reserpine, sulpiride, thioxanthenes</td>
</tr>
<tr>
<td>Hypergonadotrophic hypogonadism</td>
<td>Anti-infectious agents, cytotoxic drugs, heroine, spironolactone; surgical testicular injury; radiation therapy; anesthetic gases, boron, cadmium, carbon disulphide, heat, lead, mercury, pesticides, radiation</td>
</tr>
<tr>
<td>Asthenozoospermia</td>
<td>Atropine, antidepressants, anti-infectious agents, chlorpromazine, diazepam, local anesthetics, metoclopramide, phenolamine, propranolol; cadmium, copper, silver</td>
</tr>
<tr>
<td>Obstructive pathology</td>
<td>Deferential surgery; epididymal surgery; inguinal hernia repair; orchiopexy; prostatic surgery; vesical surgery; mercury</td>
</tr>
</tbody>
</table>
Management of the infertile couple

Female partner

- Basal body temperature

Hysterosalpingography

- Normal
- Abnormal

Endovaginal ultrasound

Evaluation of cervical mucus

Postcoital test

Serum progesterone

Male partner

Semen analysis

Diagnosis of female infertility causes

Laparoscopy

Hysteroscopy
Management of the infertile couple

Repeat semen analysis → Semen analysis → Normal values

abnormal, then consider

History → Physical examination

Intraindividual variability

Sexual abstinence before semen collection
Method of sperm collection

Type of semen abnormality

Laboratory related variability

Azoospermia

Other semen abnormalities

Retrograde ejaculation
Sperm in post-orgasm urine → no → Anejaculation
Management of the infertile couple

Azoospermia

Testicular failure

Karyotype

- abnormal
- normal

FSH

LH Testosterone

- high
- normal
- low

Androgen resistance

Clinical examination

Obstructive azoospermia

Scrotal exploration

- abnormal

Obstructive azoospermia

Testicular biopsy

- abnormal

Testicular failure

Hypogonadotropic hypogonadism

- Isolated gonadotrophin deficiency
- Specific genetic syndromes
- Suprasellar tumors
- Traumas
- CNS infections
- CNS vascular diseases
- Pituitary tumors
- Chronic illnesses
-iatrogenic causes

Sertoli-Cell-Only syndrome
- Cryptorchidism
- Orchitis (mumps)
- Testicular tumors
- Varicocele
- Testicular injury
- Testicular torsion
- Latrogenic causes
- Occupational causes

Klinefelter syndrome
- 46,XX males

Autosomal anomalies

Infections
- Congenital abnormalities
- Epididymal tumors
- Traumas
- Cystic fibrosis
- Iatrogenic causes
Management of the infertile couple

Oligo-Astheno-Teratozoospermia

- Asthenozoospermia
  - <10% motile sperms
  - Electron microscopy: abnormal axonema
  - Structural tail anomalies
  - History
  - Genital examination
  - Immunologic factor: MAR test, abnormal
  - Accessory gland infection: low testicular volume
  - Low sperm concentration
  - Azoospermia evaluation
  - Ejaculate signs: hypospermia, abnormal pH, coiled tails, leucospermia, bacteriospermia, abnormal biochemistry, abnormal prostatic fluid, abnormal ultrasound

- Oligozoospermia
  - Exclude short sexual abstinence or incomplete sperm collection
  - History
  - Genital examination

- Teratozoospermia
  - Exclude monomorphic genetic syndromes
  - History
  - Genital examination

- Partial obstruction
  - Abnormal tails
  - Abnormal heads

- Signs of genital tract obstruction
  - Varicocele
  - Abnormal prostatic fluid
  - Abnormal ultrasound
Evidence-based recommendations

Investigation of fertility problems and management strategies

- The routine use of post-coital testing of cervical mucus in the investigation of fertility problems is not recommended because it has no predictive value on pregnancy rate.

Medical and surgical management of male factor fertility problems

- Men with idiopathic semen abnormalities should not be offered anti-oestrogens, gonadotrophins, androgens, bromocriptine or kinin-enhancing drugs because they have not been shown to be effective.
- Men should be informed that the significance of antisperm antibodies is unclear and the effectiveness of systemic corticosteroids is uncertain.
- Men with leukocytes in their semen should not be offered antibiotic treatment unless there is an identified infection because there is no evidence that this improves pregnancy rates.
- Men should not be offered surgery for varicoceles as a form of fertility treatment because it does not improve pregnancy rates.

Ovulation induction

- **Polycystic ovary syndrome**
  - Women with World Health Organization Group II ovulation disorders (hypothalamic pituitary dysfunction) such as polycystic ovary syndrome should be offered treatment with clomifene citrate (or tamoxifen) as the first line of treatment for up to 12 months because it is likely to induce ovulation.
  - Anovulatory women with polycystic ovary syndrome who have not responded to clomifene citrate and who have a body mass index of more than 25 should be offered metformin combined with clomifene citrate because this increases ovulation and pregnancy rates.
  - Women with polycystic ovary syndrome who have not responded to clomifene citrate should be offered laparoscopic ovarian drilling because it is as effective as gonadotrophin treatment and is not associated with an increased risk of multiple pregnancy.
  - Women with World Health Organization Group II ovulation disorders such as polycystic ovary syndrome who do not ovulate with clomifene citrate (or tamoxifen) can be offered treatment with gonadotrophins. Human menopausal gonadotrophin, urinary follicle-stimulating hormone and recombinant follicle-stimulating hormone are equally effective in achieving pregnancy and consideration should be given to minimising cost when prescribing.
  - Women with World Health Organization Group II ovulation disorders such as polycystic ovary syndrome who ovulate with clomifene citrate but have not become pregnant after 6 months of treatment should be offered clomifene citrate-stimulated intra-uterine insemination.
  - The effectiveness of pulsatile gonadotrophin-releasing hormone in women with clomifene citrate-resistant polycystic ovary syndrome is uncertain and is therefore not recommended outside a research context.

- **Hyperprolactinaemia**
  - Women with ovulatory disorders due to hyperprolactinaemia should be offered treatment with dopamine agonists such as bromocriptine. Consideration should be given to safety for use in pregnancy and minimising cost when prescribing.

Unexplained infertility

- Women with unexplained fertility problems should be informed that clomifene citrate treatment increases the chance of pregnancy, but that this needs to be balanced by the possible risks of treatment, especially multiple pregnancy.