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Subfertility

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INTRODUCTION

Definition

A couple is regarded as subfertile if they have not achieved pregnancy after 2 years of having regular unprotected sex. This definition needs some explanation:

- To achieve pregnancy is to have vaginal intercourse with the intention of getting pregnant (so no use of condoms or anticonceptives).
- To achieve pregnancy is something other than delivering an alive baby: miscarriages, stillborns etc. are also counted as pregnancy.
- Regular intercourse means at least once or twice around ovulation each month (cycle days 11–14 in a regular cycle).
- The duration of 2 years: many couples who are normally fertile will come earlier to a clinic for investigation or advice on how to achieve pregnancy. If women have a regular cycle and are aged <35 years we do not advise starting investigations on these couples because it is not cost-effective as they still have a good chance of conceiving spontaneously.

We make a distinction between primary and secondary subfertility:

- *Primary subfertility*: a woman was never pregnant or a man never made any woman pregnant.
- *Secondary subfertility*: a woman was ever pregnant before, but is not able to conceive now, or a man ever made any woman pregnant.

We also make a distinction between infertility and subfertility:

- *Infertility*: a man or a woman is in no way able to make someone or become pregnant.

- *Subfertility*: the ability of a man, a woman or a couple to make or become pregnant is lower than 'normal', but still able to conceive. Again, we do not call someone subfertile when he/she had a (recent) miscarriage.

Because most of the time you do not yet know if a person is not able to make or become pregnant in the future it is better to speak of subfertility.

Magnitude of the problem

Sub- and infertility is a major public health problem in low-resource countries including sub-Saharan Africa (level of evidence 1), where a prevalence of between 13% and 32% is reported. In many countries motherhood is the only way for women to enhance their status in the community, and infertility is associated with marked social stigma and might be detrimental to a woman's position within the family and the community. To overcome infertility, men and women spend considerable sums of money in treatment^{1,2}.

Infertility is a serious reproductive health problem for a society, but has a low priority on the political and health agenda of low-resource countries. International and national policy makers focus on the reduction of maternal and neonatal mortality and morbidity, and family planning. Prevention of infertility, especially secondary infertility caused by reproductive tract infections, and improvement of obstetric and pediatric care in order to reduce postpartum infections^{3,4}, 'fetal wastage' and under-5 mortality, remain important interventions and should be part of integrated reproductive healthcare services as much as family planning.

PHYSIOLOGY OF THE FEMALE CYCLE

To understand disorders, investigations and treatment of infertility, it is important to study the menstrual cycle again. The cycle starts on the first day of the period (when vaginal blood loss starts) and stops on the first day of the next period. We call a cycle regular if the cycle is between 25 and 35 days: 91–97% of those women will have an ovulatory cycle⁵. We say that a woman has oligomenorrhea if the cycle is >35 days and amenorrhea if the cycle is >6 months.

You can distinguish three phases in the female cycle (Figure 1); the duration of the first half (follicular phase) of the cycle is not the same in all women. The length of the second (luteal) phase is always 14 days so ovulation takes place 14 days before the next period starts and you can only determine ovulation retrospectively.

1. *Menstruation*: discharge of the endometrium (on day 1 to approximately day 4–7).
2. *Follicular phase*: starts after the blood loss stopped. In this phase the follicle is stimulated, grows and produces estrogen. The growth of the follicle is under the influence of the hormone follicle-stimulating hormone (FSH), produced by the pituitary gland. When you make an ultrasound in the follicular phase of the cycle you will see that the endometrium is formed in three layers (Figure 2) and that a follicle is formed (Figure 3). The growth of the follicle is (start counting only if the follicle is 1 cm) approximately 0.2 cm each day and will rupture (we call this ovulation) when it is 2 cm.

Rupture of the follicle is preceded by a surge in the hormone luteinizing hormone (LH), produced in the pituitary gland. At this time, the ovum (the egg which is not visible with the bare eye) will come out of the follicle and can be fertilized.

3. *Luteal phase of the cycle*: this is the phase in which a fertilized egg (called an embryo at this stage) can settle in the endometrium. In this phase the endometrium is prepared by the hormone progesterone which is produced by the ruptured follicle (called the corpus luteum) to provide a good environment for growth and development of the embryo. On ultrasound in the luteal phase the endometrium is white and

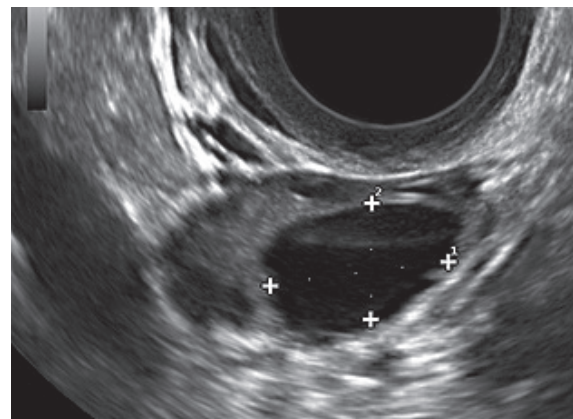


Figure 2 An ovary with more follicles. The biggest follicle which we call the dominant follicle will rupture when it is 2 cm in diameter. You can measure it with the ultrasound machine. Courtesy David van Ham

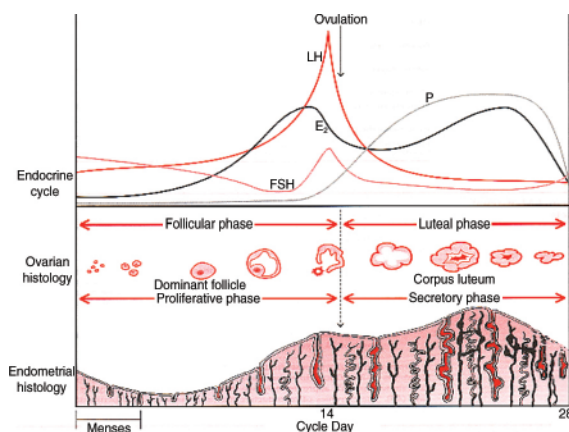


Figure 1 Schematic view of the different phases in the female menstrual cycle

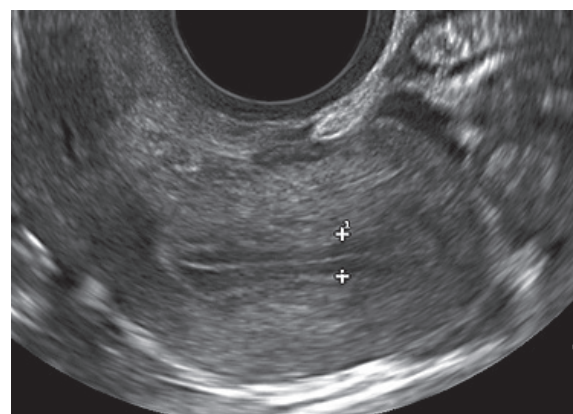


Figure 3 Endometrium in the follicular phase of the cycle: you can clearly see the triple line. Courtesy David van Ham

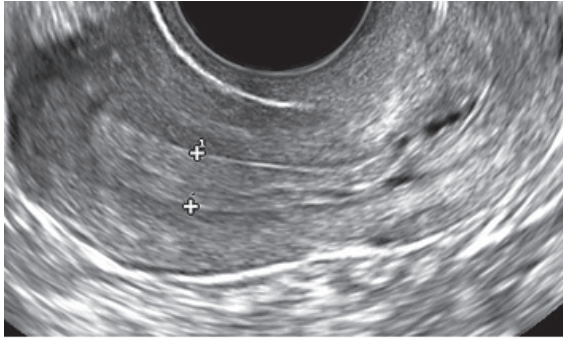


Figure 4 Endometrium in the luteal phase of the cycle: you can clearly see that the endometrium does not have triple lines anymore and has become dense. Courtesy David van Ham

is no longer triple layered (Figure 4). When the ovum is not fertilized or when the embryo is not implanted in the endometrium, the next period will start.

CAUSES OF SUBFERTILITY

Causes of subfertility could be in the woman, in the man, in both, or unexplained (Table 1). In women, the following three problems are the most common causes of female subfertility: anovulation, blockage of the tubes, cervical hostility. Rare causes are large fibroids or Asherman’s syndrome (adhesions of the endometrium after infection or curettage).

In men, poor quality semen or, rarely, sexual difficulties are the causes of subfertility.

Anovulation

A follicle which ruptures and is fertilized is critical for becoming pregnant. Most women (around 91–97%) with a regular cycle (between 25 and 35 days) will produce a follicle monthly and thus have a chance of becoming pregnant⁵. The chances for women with oligomenorrhea becoming pregnant are less. The causes of anovulation are:

- *Polycystic ovary syndrome (PCOS)*: this is a disease in which many small follicles grow (you can see it on ultrasound, per definition >12 follicles of between 2 and 9mm in each ovary, or an increase in ovarian volume >10cm³)⁶, but no follicle will become ripe and rupture. Women will have oligomenorrhea (cycle of more than 35 days) and are often (but not always) obese.

Table 1 Common causes of subfertility

<i>In woman</i>
No ovulation
PCOS
Hyperprolactinemia
Early menopause
Hypophysis/hormone abnormalities
Tubes are not patent
Hydrosalpinx
Adhesions
Proximal tube blockage
Endometriosis
Cervical hostility
<i>In man</i>
Semen not good enough
Azoospermia
Oligospermia
<i>Unexplained</i>

For an example of an ultrasound in women with PCOS, see Figure 7.

- *Hyperprolactinemia*: the pituitary gland in the brain produces too much prolactin (hormone that stimulates lactation). Typically these women will have milk from the breast and a very irregular cycle.
- *Extreme weight loss (HIV, anorexia, famine) and stress*: you can ask the patient if she lost a lot of weight recently.
- *Hormonal imbalance like hyper- or hypothyroidism*: women will have the classical symptoms of hypo- and hyperthyroidism with an irregular cycle.
- *Severe infections of the ovaries*: these can destroy the function of the ovaries entirely.

Tubes are not patent

This happens often after sexually transmitted infections (STI; see Chapter 17) and often women have a history of symptoms of STI/pelvic inflammatory disease (PID) and sometimes chronic abdominal pain. Sometimes they have a history of ectopic pregnancy. If you can make an ultrasound you often can see hydrosalpinges (see Figure 6). You can test the patency of the tubes in several ways (see section on Investigations on subfertility).

Cervical hostility

During the growth and development of a dominant follicle, that follicle produces estrogen which

changes the consistency of the cervical mucus (the mucus produced by the glands in the cervix): the mucus becomes very clear and forms threads. This only happens around ovulation. The function of this change in mucus is so that the sperm cells can swim up via the cervical mucus inside the uterus. In some women, cervical mucus does not change and stays white and is full of leukocytes: the sperm cells cannot use the mucus to swim up towards the follicle.

Semen is not good enough

The World Health Organization (WHO) have defined good sperm quality (Table 2). This does not mean that if sperm is of lower quality that it is completely impossible to make a woman pregnant. Production of sperm cells takes 3 months and is negatively influenced by high temperatures as in fever. If you find a poor sperm sample, you should repeat it after 3 months (not earlier!).

Unexplained subfertility

We diagnose unexplained infertility if all the tests are normal: the woman is ovulating, the tubes are patent, the cervical mucus is good, the post-coital test is positive (see below) and the man has good semen; however, the woman has still not become pregnant. This could be because there are many aspects in human fertility which are still not understood. However, other factors may play a role: infrequent or wrongly timed intercourse, sexual problems, intravaginal application of spermicide (washing of the vagina, often with traditional herbs, directly after intercourse). The service provider can detect such fertility-hindering factors through thorough history taking.

HISTORY TAKING IN SUBFERTILITY

A detailed history will give you directions about the cause of the subfertility. It is recommended to

Table 2 WHO criteria for normal semen

Volume	≥2.0 ml
Sperm concentration	≥20 million per ml
Motility	50% progressive motile or >25% rapid progressive motile
Morphology	≥30% normal
White blood count (WBC)	<1 million per ml

use a fixed structured questionnaire, so that you do not overlook some questions. An example of this questionnaire can be seen in the Appendix at the end of this chapter. You can also develop your own form. The important questions are:

- Duration of fertility problem: the longer the duration of the subfertility, the less likely it is that you could help this couple. For example, if a woman has a strict regular period and a subfertility of 10 years with a husband who has three children with his other wives, it is very likely that this woman has blocked tubes.
- Age (especially of woman). In older women (this does not count for men) fertility becomes a lot lower. Do not waste time and your patients' money tackling infertility problems in women over the age of 42 years.
- Ever pregnant before?
 - Alive baby (still alive?). Any history of infection around the delivery?
 - Intrauterine fetal death (IUFD). Any history of infection around the delivery?
 - Abortion (spontaneous, induced or dilatation and curettage, D&C). Any history of infection around that abortion?
 - Ectopic pregnancy. Then the other tube could be damaged as well.
- Periods and cycle
 - Cycle: from first day of period until first day of next period
 - Regular: women with a cycle between 25 and 35 days will have in 91–97% of cases an ovulatory cycle
 - Oligomenorrhea: cycle >35 days
 - Amenorrhea: cycle >6 months
 - The amount of blood loss: heavy bleeding could be a sign of fibroids.
- Galactorrhea. Women with galactorrhea often have an anovulatory cycle.
- Secondary dysmenorrhea (see Chapter 7). After PID (Chapter 17) or endometriosis (Chapter 6).
- Sexual intercourse
 - Frequency. Should be at least twice around the fertile phase of the cycle
 - Problems during intercourse. Pain (deep dyspareunia, see Chapter 6) could be a sign of PID (Chapter 17) or endometriosis (Chapter 6). Does the man ejaculate in the vagina? Does the woman perform intravaginal washings straight after intercourse (she should not

do that because this could kill or remove the sperms)?

- Weight gain or weight loss of woman. Heavy weight loss will reduce ovulation. Signs of chronic diseases like tuberculosis or AIDS? Excessive weight gain will also give anovulatory cycles and PCOS (see section on causes of subfertility).
- History of STI, PID and HIV in men and women (see Chapters 17 and 18). PID can cause blockage of the tubes. HIV with chronic infections could lead to anovulation and amenorrhea (read about special considerations for HIV-positive infertility patients in Chapter 18). History of tuberculosis.
- Having more sexual partners before or now – male and female. When women have already changed partners frequently because of subfertility it will be more likely that the cause of infertility is either anovulation or blocked tubes and not poor sperm quality.
- History of family planning methods:
 - IUD: risk of subfertility through salpingitis only around period of insertion
 - Depo-Provera®: it could take up to 1 year after stopping injections before ovulations start again
- Smoking and use of alcohol: both reduce the chances of pregnancy in men and women.
- Stress: both mental and physical stress reduce ovulation.
- History of abdominal operations or hydrocele/herniography in men. In women abdominal operations can cause adhesions. Unfortunately, many doctors still perform curettages because they think this will cure subfertility.

INVESTIGATIONS IN SUBFERTILITY PATIENTS

In low-resource settings it is usually possible to do basic subfertility examinations yourself or refer patients to healthcare facilities where they could perform the following four examinations.

Post-coital test

The post-coital test (PCT) is a test you should perform just before ovulation. For women with a regular cycle of 28 days this is on cycle day 12–14 (we start counting the cycle days on the first day of the period). Just before ovulation, cervical mucus is

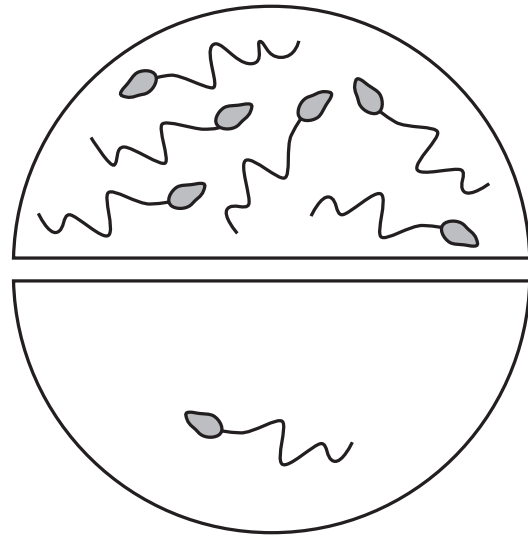


Figure 5 An example of a post-coital test under the microscope. Use the 40× ocular and look if progressive motile sperm cells are present

clear and abundant and forms threads. Production of cervical mucus is stimulated by hormones (estrogen produced in growing follicle).

Perform the PCT 9–24 h after intercourse: do a speculum examination and gently remove some mucus from the cervix and put it on a microscope slide. Examine cervical mucus for progressive motile spermatozoa using a microscope with the ocular on 40x (Figure 5). You can remove some mucus from the cervix by using a tuberculin syringe (without a needle, suck some mucus into your syringe) or use a sponge-holding forceps (just grasp some mucus in your forceps). Put the mucus on a microscope slide and use a covering slide.

- The PCT is positive if one or more progressive motile sperm is seen per high-power field (40×).
- When the mucus is not clear and you see many dead sperm cells: the timing of the PCT could be wrong (too long before or already after ovulation or it is an anovulatory cycle) or the woman may have a cervical mucus problem called cervical hostility. In all these cases you should repeat the PCT later in this cycle and when still not positive, in the next cycle. If you have an ultrasound machine you could check if a follicle is present and measure the size of the follicle.
- The mucus is clear and abundant, but no sperm cells are seen or no progressive motile sperm

cells are present. This could be a sperm problem: repeat the PCT in the next cycle or do a sperm analysis (see later).

Please note: no research has been done on the PCT in low-resource settings and many gynecologists prefer to perform a sperm count. However, a sperm count is more difficult to perform and you need a well-equipped laboratory to have reliable results. The UK Royal College of Gynaecologists (RCOG) guidelines do not mention anything about PCT and it is largely because the practice in the UK, and the West for that matter, relies very heavily on the support network of the laboratories and *in vitro* fertilization (IVF) units which can give far better prognostic information about the pregnancy outcome results of the tests.

Hull *et al.*⁷ maintain that 'penetration of mucus by spermatozoa is an essential test, more discriminating than standard semen analysis provided that valid conditions are ensured' and this was further supported by several authors including Collins *et al.*⁸ who found positive correlation between the number of motile spermatozoa observed in the mucus and pregnancy rates. There has however been a steep decline in the enthusiasm for this test because of lack of validity^{9,10}.

In low-resource countries a case could be made for this test on the basis that it would be easier to set it up with very low overheads than say a fully equipped laboratory, which will also require additional trained personnel. A PCT could be done by any clinical staff already available and will require very little by way of training and equipment.

Ultrasound in subfertility

You can use the ultrasound to help you to make a diagnosis in subfertility. It is very nice if you have a good ultrasonographer in your health facility or if you are one or become one yourself! What can you see on a (vaginal) ultrasound in subfertility? For subfertility ultrasound please have a look at the following:

- Endometrium:
 - Triple line endometrium (Figure 3): sign of follicular phase of the cycle (before ovulation)
 - Dense white endometrium (Figure 4) without the triple line phenomenon: after ovulation, or no ovulation occurred.
- Hydrosalpinges (Figure 6): normally you do not see the tubes on ultrasound.

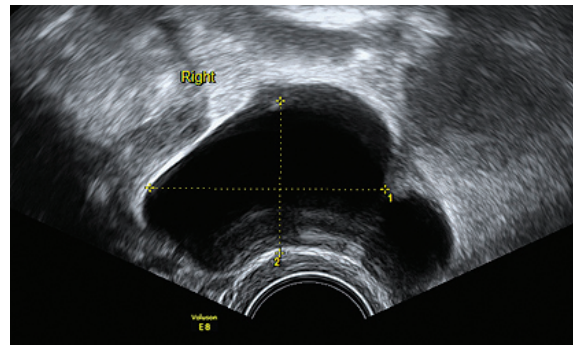


Figure 6 An example of a hydrosalpinx seen on ultrasound. Courtesy Esther Westen

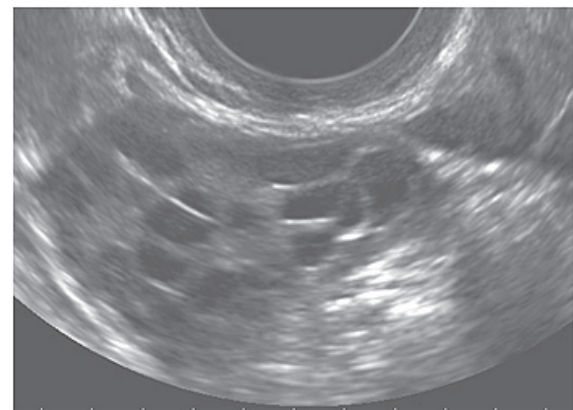


Figure 7 An ultrasound of a woman with polycystic ovary syndrome: you can see the follicles looking like a necklace of small follicles of the same size. Courtesy David van Ham

- Follicle size (see Figure 2): we know that starting from approximately 10 mm, the dominant follicle will grow 2 mm each day. So you could predict when ovulation will take place and plan the date of a PCT.

You can use the ultrasound for:

- Detection of follicle (Figure 2)
- Abnormal ovarian cysts
- Hydrosalpinx detection
- Fibroid detection
- Timing of PCT: follicle at least 16–18 mm and triple line endometrium
- PCOS (see Figure 7)

Semen analysis

A sperm sample is obtained by masturbation and collected in a clean glass container. It is important

to collect the entire sperm sample, so please realize it is very difficult to collect an entire sperm sample in a test tube, please advise use of, for example, a urine collection bottle. If no containers are available at the hospital the clients could boil any glass container in water at home and use this. The specimen should be collected <1 h before analysis. Speak to your lab technician about whether he/she is able to perform a semen analysis and if not try to arrange training.

It is not necessary to perform semen analysis in every subfertile couple: only when the PCT remains negative should you perform a semen analysis. The quality of semen fluctuates a lot: after a period of fever it takes 3 months for semen to normalize. Only when no sperm at all are found in three specimens with at least 3 months in between is there absolute infertility. When the sperm count is abnormal you should repeat it after 3 months⁵.

Table 2 shows normal semen analysis according to the WHO criteria. When the semen is a bit less than the WHO criteria it does not mean that this is the direct cause of subfertility – as already mentioned, the quality of semen fluctuates a lot and many times more than one factor makes a couple subfertile!

Hysterosalpingography

A hysterosalpingograph (HSG) is an X-ray with contrast fluid to detect abnormalities in:

- Uterine cavity
- Tubes
- Adhesions

Disadvantages of HSG are that it often gives false-negative or false-positive results and it needs some specialized X-ray equipment that might not be present in all facilities. In addition it should be noted that the X-ray contrast solution is rather expensive.

To prevent infections and reduce pain: one night before and 1 h before HSG give 200 mg doxycycline and 50–100 mg diclofenac. The procedure is as follows: on the X-ray table you do a speculum examination and grab the cervix with a tenaculum. Clean the cervix with antiseptic and introduce a hystero-phore or a small catheter. The big advantage if you have a hystero-phore is that this instrument will close the cervix and no fluid will flow backwards into the vagina. After the instrument has passed the internal cervix, attach the

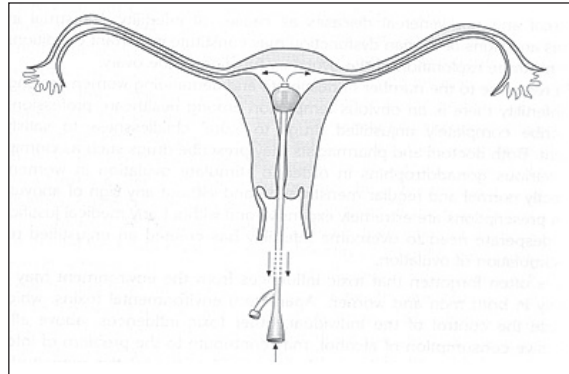


Figure 8 Diagram illustrating a hysterosalpingography

syringe with X-ray contrast solution to it and slowly inject 20 ml of the solution into the uterus. This part will be painful. Make an X-ray during the injection, just after the injection and 1 min after injection of the contrast fluid. Then remove all the equipment in the order – last in first out (Figure 8).

If you do not have HSG facilities but you have/are a good ultrasonographer, try to visualize the tubes and check their patency by using normal saline: insert a small intrauterine cannula or catheter and slowly rinse the catheter with maximum 50 ml of normal saline during which you make a vaginal ultrasound: if you see the saline filling the tubes and flowing into the abdomen and spreading through the whole pelvis, you know that the tubes are patent and it is unlikely that adhesions cause this infertility (level of evidence 3). You should only do this method under aseptic conditions, and one night before and 1 h before the procedure you should administer 200 mg doxycycline and 50–100 mg diclofenac. Both HSG and hydrotubation are reported to be successful in achieving pregnancies in selective patients: thin peritubal adhesions might be opened (level of evidence 3)¹¹.

Schistosomiasis and infections

In some areas in the world schistosomiasis could be a cause of infertility. Detect schistosomiasis in urine or cervix biopsy (see Chapter 9) and if positive, give appropriate treatment.

If you suspect gonorrhoea or a *Trichomonas* infection: do a high vaginal swab to exclude pathogenic microorganisms and treat accordingly (see Chapter 17 about STI).

In some countries tuberculosis is endemic and causes infertility. It is very difficult to detect

endometrial tuberculosis. This could be done after endometrium sampling using the smallest cannula from manual vacuum aspiration and special pathology staining.

DIAGNOSIS OF SUBFERTILITY

After you have done the history taking and specific examination you can diagnose the cause of the subfertility.

Some causes you can treat others not. It is always important if you are a health provider to give support to your patients: give a clear explanation of the cause of the disease and in the meanwhile also give an opportunity for the patients to show their concern and their emotions. For many men and women the inability to procreate gives considerable grief and stress, not only to themselves but also to their social environment. If you address these issues you could help your patients cope with their difficult situation.

TREATMENT OF SUBFERTILITY IN LOW-INCOME COUNTRIES

Some of the subfertility treatment is possible on district or regional level in most low-income countries. Some of the infertility treatment like IVF is only possible on a national level because it is expensive and needs more expertise. In this book we will only talk about the treatment you could provide with district and regional level facilities. Table 3 gives an overview of the conditions you could treat; the conditions you cannot treat are shown in bold.

The decision on whether to start a subfertility treatment clinic is dependent on the situation in your health facility – the magnitude of the subfertility problem, the human resource situation at your facility, the distance to other subfertility clinics, poverty of your population etc. But now you have the knowledge about subfertility, you could start with treatment of the ‘easy’ causes of subfertility – anovulation because of PCOS and because of hyperprolactinemia. More difficult treatment such as intrauterine insemination (IUI) and surgery you can always add later when you have acquired the skills and when the need is there! But be careful: usually once people know that your clinic is providing any kind of treatment for subfertility, many will come, as subfertility is a big problem almost everywhere in the world and childless people have suffered a lot and are desperate for help.

Table 3 Overview of possible treatments for various infertility disorders; conditions in bold cannot be treated

<i>In woman</i>	
No ovulation	PCOS: ovulation induction with clomiphene citrate
	Hyperprolactinemia: bromocriptine
	Early menopause
	Hypophysis abnormalities
<i>Tubes are not patent</i>	
	Hydrosalpinx: refer for surgery or IVF
	Adhesions: refer for surgery or IVF
	Proximal tube blockage : refer for IVF
	Endometriosis: sometimes surgery COC or Depo-Provera (see Chapter 6)
	Cervical hostility: IUI
<i>In man</i>	
Semen not good enough	
	Azoospermia
	Oligospermia: IUI
<i>Unexplained</i>	
Superovulation and IUI or refer IVF	

IVF, *in vitro* fertilization; COC, combined oral contraception; IUI, intrauterine insemination

Flowchart for subfertility

The flow chart in Figure 9 is a good tool to use in decision-making in infertility patients. Please copy the card and put it on the wall. In the flowchart you see that the first decision is based on the regularity of the cycle. Women with a regular cycle should have PCT, ultrasound and HSG early in the work-up. Women with an irregular cycle should first have had ovulations for at least 6 months, before you perform a HSG.

Treatment of anovulation caused by polycystic ovary syndrome

When the woman is severely overweight, she first should lose weight. Many women with PCOS start ovulating again when they lose about 10–20% of their weight. In order to reach this weight loss, patients should combine a low-calorie diet with exercise. Make a plan with your patient: give her a low sugar, low alcohol and low-fat diet and let her exercise 1 h per day. Weigh her monthly to monitor progress.

You can induce follicle growth (level of evidence 1) with clomiphene citrate (CC). Give 1 tablet CC

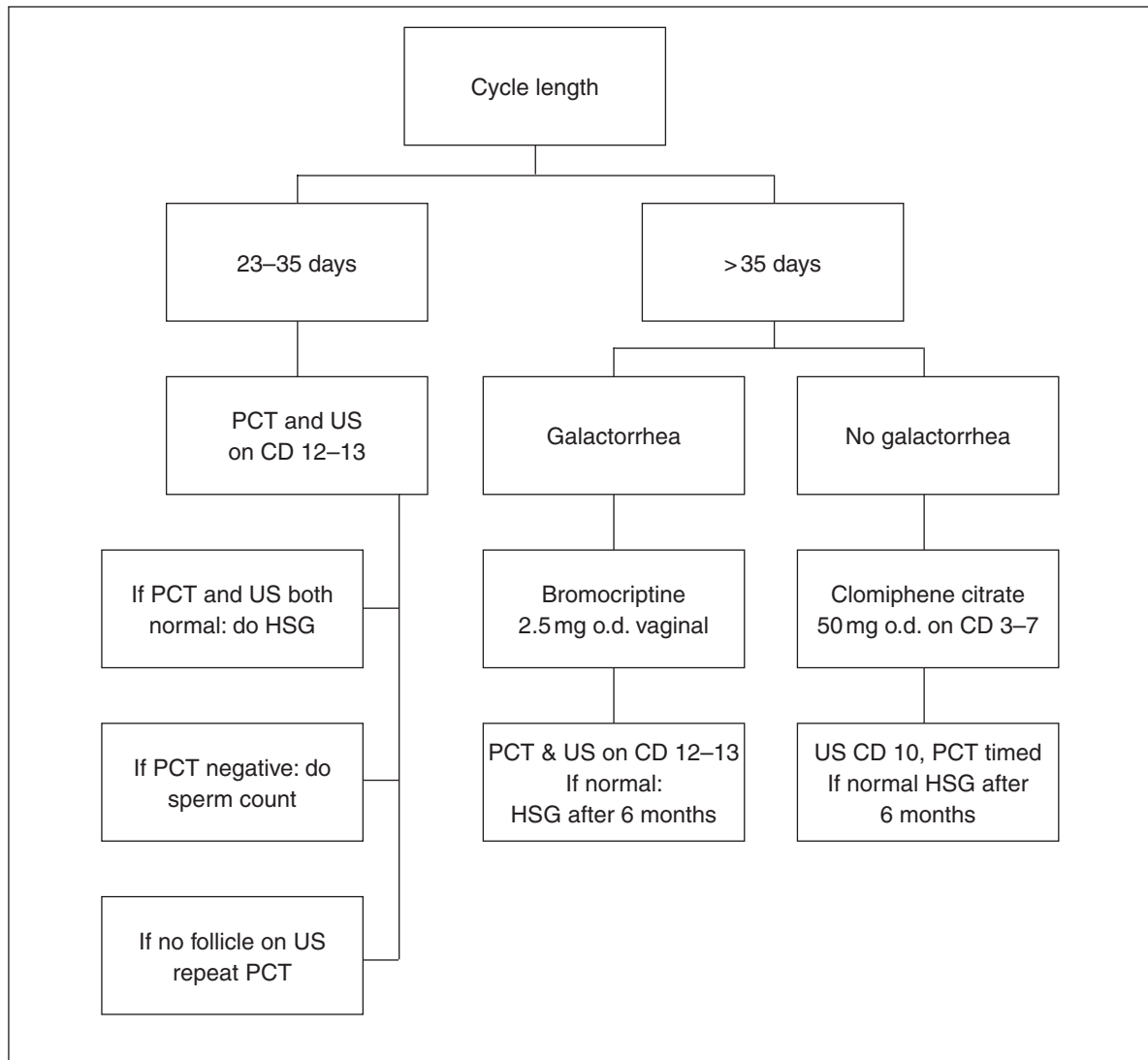


Figure 9 Flowchart for subfertility. PCT, post-coital test; US, ultrasound; CD, cycle day; HSG, hysterosalpingography

50 mg on cycle day 3–7 (again: day 1 is the day the period starts, the woman has to use only five pills per month, and she should not wait until menstrual flow stops before taking them). You must monitor multiple follicle growth (twins, triplets etc.) with ultrasound during the first cycle: CC can give multiple follicles and so multiple pregnancies! When more than two follicles are developing: advise the couple to have only protected intercourse (condoms) this cycle. Twins and triplets in a low-resource setting have a high maternal morbidity and perinatal morbidity and mortality. When too many follicles are growing: start the next cycle with half a tablet of CC 50 mg on cycle day 3–7.

When no follicles are growing when using 1 tablet CC 50 mg on day 3–7, next cycle give her 2 tablets CC 50 mg on cycle day 3–7. When no follicles are growing on 2 tablets: next cycle prescribe 3 tablets CC 50 mg on cycle day 3–7. This is the maximum dose. If still no ovulation occurs, start with continuous metformin 500 mg b.d. for 3 months combined with 3 tablets CC 50 mg on cycle day 3–7. If still no follicle forms, you could refer your patient to a fertility specialist.

Monitor PCT for cervical hostility during the first ovulatory cycle: CC induces cervical hostility in some patients! You can time the PCT and ovulation because you know that a follicle >10 mm will

grow 2mm each day. Normally follicles rupture when they are 20mm. When you give CC, they can grow a bit bigger and ovulation can be a few days later. So instruct your patients to have intercourse every second day during the second half of the cycle. The maximum number of months you should prescribe CC is 6 months. If a couple is by then still not pregnant, more examinations should be done: make a HSG or refer the patient.

Treatment of hyperprolactinemia

Hyperprolactinemia stimulates the breast to form milk and inhibits follicle growth. Bromocriptine 2.5mg o.d. blocks the production of prolactin in the pituitary gland adenoma and follicles can develop normally again. Bromocriptine has many side-effects but if you administer the (oral) tablets vaginally the side-effects are mild. You should prescribe it for a longer time: it takes a few weeks to months before the cycle is normalized again. When no ovulation occurs after 3 months: double the dose. When a woman becomes pregnant she should stop taking bromocriptine.

Remember: pituitary gland adenomas could also cause visual symptoms; patients will complain about bad peripheral vision. When your patient has these symptoms you should refer her to a neurologist!

Treatment of hydrosalpinx and adhesions

If possible, refer your patient for surgical treatment (microsurgery) or IVF.

Treatment of cervical hostility and male subfertility

The treatment of cervical hostility should start with STI treatment including chlamydia. Counsel and test both partners for HIV because the technique we will describe could transmit HIV from the man to the woman. If treatment of STI does not improve the PCT, IUI with washed semen is the next step. This technique is based on the fact that if you bring sperm cells artificially into the uterus, you by-pass the cervix and you bring the sperm cells near to the follicle. This technique is also suitable for men with oligospermia. But sperm cell count should be reasonable: sperm VCM should be minimal 1 million (VCM = volume × concentration × motility).

It is a simple swim-up technique. First, monitor the cycle with ultrasound until the follicle is around

18mm. Wash the sperm – you could do this in very expensive fluid, but it is also possible to use the serum of the woman. Collect the fresh sperm specimen [produced <1 h previously in a sterile (boiled) container via masturbation]. Work with a strictly sterile technique. Collect 5–10ml blood of the woman. Rest the blood to clot for 15 min. Centrifuge for 10 min and put the serum in a test tube. Mix the sperm of the man with the blood serum of the woman: add 1–2ml of serum of the woman to the fresh semen of the man in a test tube and mix. Incubate this mixture for 60 min in a stove at 37°C at an angle of 45°. The sperm cells will swim up and most will be just above the separation plane. Use a sterile syringe with a big needle or sterile pipette to aspirate. Try to get a maximum 0.5 ml of the serum with the sperms which swam up and immediately check one drop of sperm under the microscope to count progressive motile sperm cells. Put the patient in the lithotomy position, insert a speculum and use a small catheter (ideally an IUI catheter, but you could improvise for example with a baby nasogastric tube) and pass the tube via the cervical os into the uterus and inject the sperm-serum specimen in the uterus. Withdraw the catheter, remove the speculum and let the woman lie on her back for 15 min.

The success rate of this technique in selected patients (with proven patent tubes and an ovulatory cycle) is reported in developed countries to be about 8% per cycle. You could use the swim up technique for:

- Cervical hostility.
- Oligospermia when the VCM (volume × concentration × motility) of the sperm is at least one million.
- In treatment of unexplained subfertility with patent tubes: you could combine CC with IUI. We call this ‘mild ovarian hyperstimulation’ and the goal of this is to have two or three follicles of >16mm on ultrasound and to bring sperm cells as close as possible to improve the chances for fertilization of the follicles, but beware of multiple pregnancies. When the follicles are >16mm you give the woman an injection of 5000IU of human chorionic gonadotropin (hCG), if it is available, to induce ovulation and the next day you do the IUI with washed semen. Nevertheless the last technique is a rather complicated process and you should have a good

fertility clinic in place before you start: you need an ultrasound, a HSG, medicines like CC and hCG injections (need to be refrigerated), a good working laboratory and a dedicated staff who is willing to perform the procedure on the day before ovulation even on weekends and during holidays.

- For IUI in HIV-positive couples see Chapter 18.

PREVENTION OF SUBFERTILITY/ CHILDLESSNESS

In order to prevent infertility you should be aware of the following: about one-third of the infertility is caused by PID and STI. So to prevent infertility – condomize!

Another major cause of infertility is unskilled abortion. It is safer for women to use misoprostol (see Chapter 13) to induce abortion in cases of unwanted pregnancies than to use an unskilled abortion provider or to induce abortion herself by the use of branches, herbs etc. When PID or post-abortion infection is diagnosed the administration of appropriate antibiotics could save the fertility. The sad consequence of low-level maternal/obstetric and under-5 healthcare is that many children die perinatally and in early childhood. The improvement of healthcare for women and children in low-resource settings including the prevention of HIV and STI and reproductive tract infections will decrease unwanted childlessness. Community sensitization on the causes and treatment options of subfertility is an important a tool to raise awareness on the prevention of subfertility, childlessness and abortion.

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APPENDIX

History and examination/investigation in infertility patients

See following pages for examples of record sheets for history taking and the results of examination.

Identification number:

Date:

Woman

Name:

Age:

Address:

Job:

Which school finished?

Gravidity Parity

Living children

Abortion spontaneous

Abortion D&C

Ectopic pregnancies Y/N

Specify:

Year of last pregnancy

Conclusion: Primary or secondary infertility

Married Y/N

Lives together with husband Y/N

Previous marriages . . . times Y/N

Children from other relationship/marriage? Y/N No.

History of using anticonception Y/N

Specify which & when

Method:

Year: Duration:

Since when trying to become pregnant: Month/year:

History of STI or PID Y/N

History of fever after abortion Y/N

History of fever after childbirth Y/N

HIV test ever done Y/N If Yes: date ... - ... - ...

Last menstrual period first day: ...- ... -...

Cycle regular Y/N

How many days from first day of one period to first day
of other period: . . . days

Dysmenorrhea Y/N

How many days does period last: . . . days

Galactorrhea Y/N. If yes examine!

Sexual problems Y/N

Pain during intercourse Y/N

Intercourse frequency . . . times/week

Is woman aware of fertile days? Y/N

Gynecological surgery Y/N

Specify:

Chronic diseases:

Use of medicines:

Previous infertility examination/treatment: Y/N

Specify what and when:

Man

Name:

Age:

Address:

Job:

Which school finished?:

Does husband travel a lot? Y/N Specify:

Number of children

Living children

Ever made a woman pregnant Y/N

Conclusion: Primary or secondary infertility

Married Y/N

Previous marriages . . . times Y/N

Children from other relationship/marriage? Y/N No.

History of STI Y/N

History of epididymitis Y/N

History of mumps Y/N

HIV test ever done Y/N If Yes: date ... - ... - ...

Sexual problems Y/N

Hernia or urological surgery Y/N

Specify:

Chronic diseases:

Use of medicines:

Chronic diseases:

Use of medicines

Previous infertility examination/treatment: Y/N

Specify what and when:

GYNECOLOGY FOR LESS-RESOURCED LOCATIONS

Example of a results sheet for subfertility examination

Results

Ultrasound 1 Date: ...- ... - ...
Follicle ... mm and endometrial thickness ... mm on CD
Endometrium triple line Y/N

Ultrasound 2 Date: ...- ... - ...
Follicle ... mm and endometrial thickness ... mm on CD
Endometrium triple line Y/N

Ultrasound 3 Date: ...- ... - ...
Follicle ... mm and endometrial thickness ... mm on CD
Endometrium triple line Y/N

Conclusion: ripe follicle on CD

Post-coitus test 1 and examination:

Normal cervix: Y/N
Ratio: nulligravid/multigravid
Normal PVE Y/N
Normal female external genitals Y/N
Normal female body hair Y/N
If any abnormality, specify:
Cervical mucus: clear Y/N Making threads Y/N
Spermatozoa seen Y/N
Progressive motile spermatozoa seen Y/N
Conclusion: PCT 1: +/- timing O.K.: Y/N

Post-coitus test 2:

Cervical mucus: clear Y/N Making threads Y/N
Spermatozoa seen Y/N
Progressive motile spermatozoa seen Y/N
Conclusion: PCT 2: +/- timing O.K.: Y/N

Post-coitus test 3:

Cervical mucus: clear Y/N Making threads Y/N
Spermatozoa seen Y/N
Progressive motile spermatozoa seen Y/N
Conclusion: PCT 3: +/- timing O.K.: Y/N
Conclusion: PCT: +/-

HSG 1 Date ...- ... - ...

Uterine cavity:
Tube left:
Tube right:
Conclusion: HSG: normal/abnormal

High vaginal swab: normal/abnormal

Specify:
Treatment:

Urine/cervix biopsy for schistosomiasis: +/-

Treatment:

Final conclusion:

Sperm count 1 Date: ...- ... - ...
..... ml
..... million
..... % abnormal
..... % progressive motile
Conclusion sperm count 1: normal/abnormal

Sperm count 2 Date: ...- ... - ...
..... ml
..... million
..... % abnormal
..... % progressive motile
Conclusion sperm count 2: normal/abnormal

Sperm count 3 Date: ...- ... - ...
..... ml
..... million
..... % abnormal
..... % progressive motile
Conclusion sperm count 3: normal/abnormal

Conclusion sperm: normal/abnormal