

SUBFERTILITY I: ITS MANAGEMENT IN GENERAL PRACTICE

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This article examines the causes of subfertility and how they can be managed in general practice. The second article, to appear in the next issue, will examine the role of the hospital specialist and the treatment options now available.

SUMMARY

Subfertility is a common complaint which is often poorly managed within the health service. Its investigation and management is relatively simple and most of it can be undertaken in general practice. The role of the hospital specialist can then be limited to investigating tubal patency and undertaking the more complex forms of treatment.

DEFINITION

Subfertility can be defined in a number of ways. Patients will define it as not getting pregnant quickly enough, while the medical definition relies on statistical data such as the Cumulative Conception Rate (figure 1). This shows the number of couples who can be expected to achieve a pregnancy with the passage of time, and has a 95%ile of about two years – hence the old idea of not investigating any couple until they had been trying to achieve a pregnancy for that time.

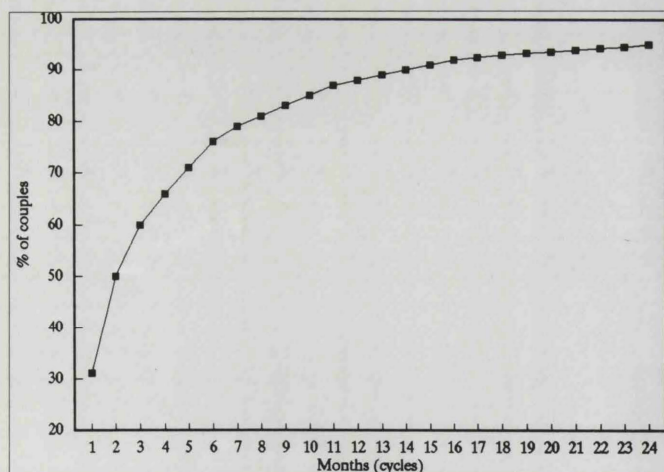


Fig 1 – Cumulative Rate of Conception¹

INCIDENCE

Many studies of the incidence of subfertility have been flawed, in that they may have dealt with a hospital-based population or been produced by pressure groups wanting an improvement in the quantity and quality of service provided. Most recent estimates suggest that about one couple in ten is affected by subfertility².

AETIOLOGY

To achieve a pregnancy a couple require:

- ovulation to occur
- spermatogenesis to occur
- spermatozoa to appear in the ejaculate
- intercourse to occur satisfactorily at the correct time in the menstrual cycle
- normal cervical mucus to be present
- healthy, patent fallopian tubes
- that no anti-sperm antibodies are present
- a suitable intra-uterine environment for implantation to occur.

Failure of one or more of these may lead to subfertility. It should be remembered that it is common for more than one problem to exist in a couple. Figure 2 shows the comparative frequency with which the causes of subfertility are found in a population.

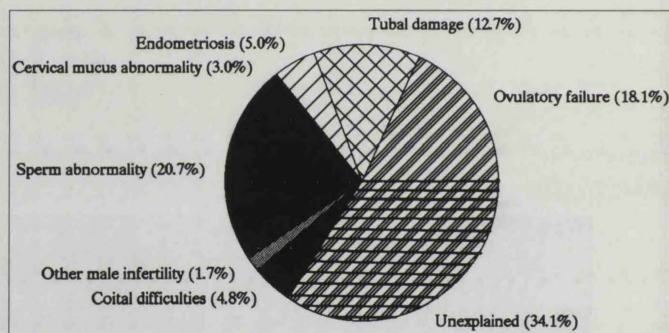


Fig 2 – Causes of Subfertility³

PRESENTATION

This is usually by the female attending her general practitioner (GP) complaining that she has not conceived despite some time without using contraception. Less commonly the couple attend, and very rarely the male attends for advice on his own.

INITIAL MANAGEMENT

As failing to achieve a pregnancy involves both partners they should be interviewed together, and jointly involved in their care from then on. In many cases they are registered with different practitioners, but this does not prevent such an approach. On occasion the couple may find it helpful for one of them to transfer to the other's GP. As with all consultations the aim is to achieve a diagnosis, which is best achieved by:

- taking a proper history
- examining the couple (where relevant)
- performing the **relevant** investigations necessary to confirm the presumptive diagnosis.

Failure to follow this basic approach leads to much unnecessary delay and frustration for the couple, as well as wasting scarce resources.

Occasionally there is some benefit in seeing each of the couple separately to discuss aspects of their past history of which the other is unaware, though this can usually be done whilst examining each of them in turn.

HISTORY

The duration of their perceived subfertility should be assessed, and due allowance made for those cycles when conception was impossible due to absence of the male around mid-cycle (e.g. working away from home). Any previous pregnancies for both partners should be documented, with particular regard to their outcome in the female partner.

The frequency of sexual intercourse should be ascertained, and any difficulties the couple have should be explored. It is surprising how many apparently well-educated couples have little or no idea as to how conception occurs, and the limited time each cycle within which intercourse should take place for it to be possible.

The male's occupation may lead to exposure to toxins which reduce his fertility – e.g. carbon disulphide (rayon), lead, radiation.

Many drugs may also affect his fertility – e.g. sulphasalazine, nitrofurantoin, cimetidine, spironolactone, testosterone injections, cytotoxic agents.

The female's current menstrual history is vital, with a regular cycle and *mittelschmerz* suggesting ovulation while oligomenorrhoea makes it unlikely. Recent changes in her weight may also inhibit ovulation. These points are summarised in **table 1**, and can be produced as an outpatient-referral questionnaire⁴.

HIM	BOTH	HER
Past medical	Duration	Past medical
Occupation	Previous pregnancies	Menstrual
Drugs	Intercourse	Drugs
Alcohol		Age
Tobacco		

Table 1 – Main features in the history

EXAMINATION

The female's weight (in Kgs) and height (in Ms) should be recorded and the Body Mass Index (B.M.I. = Wt/Ht^2) calculated. Where this is outside the normal range (19-25) she should be encouraged to correct it, particularly if she is overweight as this not only suppresses ovulation but also hinders her body's response to treatment.

Her blood pressure and hair distribution should be noted, along with her secondary sex characteristics. In most cases there is very little to be gained from performing a pelvic examination, unless her history suggests that some anatomical abnormality exists or if the opportunity is to be taken to perform a cervical smear.

The male genitalia should be examined to confirm the testes are of normal size and located within the scrotum. Any varicocele or epididymal cysts should be noted, and hypospadias excluded.

Table 2 summarises the relevant points of the examination.

HIM	HER
Testicular size/location	B.M.I.
Varicocele	Hirsutism
Epididymal cysts	2° sex characteristics

Table 2 – Main features of the examination

INVESTIGATIONS

These will be determined, at least in part, by the presumptive diagnosis gained from the history. The urgency with which they are undertaken is guided by:

- the duration of subfertility
- the likelihood of an abnormality being found
- the age of the female (whose fertility declines significantly after 35 years).

Both partners should be investigated, even if an obvious cause exists in one of them, as dual pathology is often found.

Initial

The basal body temperature chart (**figure 3**) has a role in general practice, though not as a means of confirming ovulation. It is used to:

- monitor the menstrual cycle – is it really regular?
- monitor how often, and when, intercourse occurs.
- fill in time when the couple either have not been trying long enough to warrant further investigation or are waiting for a hospital appointment.

The charts have no further value after three menstrual cycles.

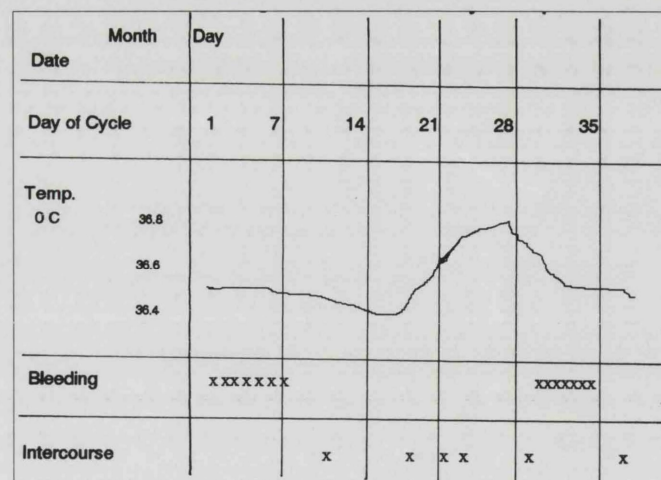


Fig 3 – Basal Body Temperature Chart

The female's immunity to rubella should be confirmed, and it is useful to check her blood group at the same time (lest she miscarry once pregnant).

Ovulation is assessed by measuring the serum progesterone in the mid-luteal phase – i.e. one week before

menstruation occurs (**figure 4**). The level usually taken as indicative of ovulation is $>20\text{nmol/L}^4$. If a low result is achieved the date of the subsequent period should be ascertained to ensure the sample was correctly timed, in which case the test should be repeated as fertile women often have cycles in which they do not ovulate.

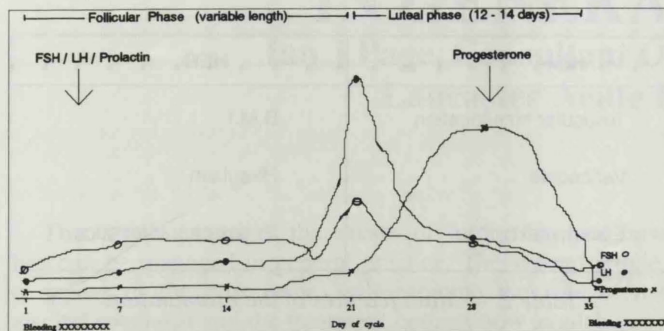


Fig 4 - Hormonal changes in a 35 day menstrual cycle (with suggested timing of blood samples).

Semen analysis (MFT) should be performed on two separate occasions, usually after a few days' abstinence from intercourse. The normal values⁵ are shown in **table 3**. Abnormal values (**table 4**) are often associated with reduced ability of the spermatozoa to fertilise ova, particularly when oligoasthenoteratospermia (OATS) is found. This has profound implications when advising which treatment should be tried.

Liquefaction	within 60 minutes of ejaculation
Volume	2mls or more
pH	7.2 - 7.8
Sperm concentration	$20 \cdot 10^6/\text{ml}$ or more
Total count	$40 \cdot 10^6/\text{ml}$ or more
Motility	$>50\%$ with forward progression
Morphology	$>50\%$ normal forms
White blood cells	$<1 \cdot 10^6/\text{ml}$
MAR test	$<10\%$ sperm with adherent particles

Table 3 - Normal values in semen analysis⁵.

Oligospermia	$<20 \cdot 10^6$ sperm/ml
Asthenospermia	$<50\%$ sperm with forward progression
Teratospermia	$<50\%$ sperm with normal morphology
Oligoasthenoteratospermia	all 3 parameters above
Azoospermia	No spermatozoa in ejaculate
Aspermia	No ejaculate

Table 4 - Nomenclature of semen variables⁵.

The mixed agglutination reaction (MAR test) should also be performed by the laboratory to exclude anti-sperm antibodies in the male.

The post-coital test (PCT) remains controversial but confirms deposition of semen on the cervix, and is an in-vivo

test of sperm survival. Although frequently undertaken by hospital clinics I believe it is eminently suitable for general practice. It should be performed just prior to ovulation and requires a 400x microscope. The couple are asked to have intercourse as usual on the day before ovulation is anticipated. The female is asked to avoid bathing (though showers are acceptable) and to attend for the test some 12 hours later. A sample of endocervical mucus is taken, and 5 or more actively-motile spermatozoa should be seen per field.

A normal result requires no further action. If it is abnormal it should be repeated with particular regard to the timing of the test within the menstrual cycle. The use of urinary LH detector kits (e.g. Clearplan) to look for the pre-ovulatory surge is often helpful in these cases.

Secondary

If the initial investigations are normal no secondary tests are required.

Azoospermia and severe oligospermia (<10 million/ml) should be further investigated by measuring the male's FSH. A level more than twice the upper limit of normal implies testicular failure⁶ for which there is no treatment. A normal level suggests the need for referral for further assessment by testicular biopsy and vasogram, to exclude ejaculatory duct obstruction. Mild oligospermia and other abnormalities may benefit from specialist assessment and further investigation. If the female is not ovulating regularly (every 4 - 5 weeks) then blood should be taken in her **early proliferative phase** (**figure 4**) to measure FSH/LH/Proactin and assess thyroid function. Any abnormalities should be referred for further evaluation as necessary. There is no diagnostic gain from pelvic ultrasound at this stage.

Tertiary

These investigations will usually require hospital resources and will be discussed in greater detail in the next article. It is recommended that they should be organised through a dedicated subfertility clinic⁴. They are mentioned briefly here to complete the overall outline of management.

Tubal patency can be confirmed by either hysterosalpingogram (HSG) or laparoscopy and dye insufflation. The latter has the advantage of allowing direct inspection of the pelvic organs, but the disadvantage of requiring a general anaesthetic. Ultrasound is only of value in the general practice setting if examination reveals a pelvic mass. In the hospital setting it may be used to diagnose polycystic ovaries, and to monitor follicular development and rupture (and so, by implication, ovulation).

Testicular biopsy and vasography can be performed to see if the testes are actually producing spermatozoa (which might be usable for insemination) and to delineate any obstruction which might be amenable to surgery.

DIAGNOSIS

This can be achieved within four months of a couple presenting to their GP. Within that time ovulation can be confirmed or excluded, the semen assessed in-vitro (MFT) and in-vivo (PCT) and tubal patency demonstrated.

Unfortunately it usually takes much longer due mainly to the long wait to be seen at hospital. It is therefore more practical (when the out-patient wait is more than four months) to refer a couple as they present, and then undertake

the other investigations. Copies (not a resumé) of the results, and any subsequent treatment given by the GP, should be forwarded to the hospital before the appointment.

SECONDARY MANAGEMENT

As mentioned earlier, management requires a thorough history to see if a problem really exists and whether or not it requires investigation/treatment. Simple education regarding the amount of time required and the factors necessary to achieve a pregnancy (see above) may be all that is necessary. Where specific advice is given it should be up-to-date and of proven value in increasing pregnancy rates, rather than in amending investigation results. This particularly applies to advice regarding the frequency and timing of intercourse. As the ovum can be fertilised only for about 24 hours after ovulation, and healthy spermatozoa can be detected in the female up to 72 hours after intercourse, it follows that intercourse every 2 – 3 days should ensure that spermatozoa are always available at ovulation for fertilisation to occur. No benefit, in terms of improved pregnancy rates, has been demonstrated by advising couples to *restrict* intercourse to the mid-cycle period. Such advice often produces stress within a relationship and should therefore be abandoned.

The use of ovulation test kits (urinary LH detection) has not been shown to improve pregnancy rates and so cannot be commended, although they are of value for specific investigations and treatment.

TREATMENT

Ovulatory Disorders

Where anovulation is thought to be related to an abnormal BMI the female should be encouraged to correct this herself. Induction of ovulation is less successful if this is not done.

In the absence of an underlying disorder treatment can be started in general practice with clomiphene citrate. Dosage regimes vary but one frequently used is 100mg daily from days 2 – 6 of the menstrual cycle. Pelvic examination has been recommended before starting Clomiphene, but this is not necessary in practice, as the risk of inducing severe ovarian hyperstimulation syndrome (OHSS) with it is miniscule. Having started treatment ovulation should be confirmed by measuring the mid-luteal progesterone level. Failure to achieve ovulation with this regime requires hospital referral and management.

Where polycystic ovarian syndrome (PCO) has been diagnosed on the basis of an elevated LH:FSH ratio (>3:1) in the early proliferative phase, coupled with hirsutism and an increased B.M.I., treatment with Clomiphene can still be instituted, though it is less successful.

Hyperprolactinaemia (two levels >1000 I.U./ml) requires referral to exclude a prolactinoma, followed by treatment with Bromocriptine. Treatment is usually stopped during pregnancy.

Abnormalities of thyroid function should be fully investigated and treated, often leading to restoration of ovulatory cycles and subsequent pregnancy.

Semen Disorders

Where a specific anatomical abnormality is thought to be the cause of an abnormal MFT the male should be referred

for specialist opinion and treatment. In the absence of a definite diagnosis of the underlying cause treatment becomes empirical, and its value is debatable. A small study in 1954⁷ showed scrotal cooling to improve sperm numbers and quality, but did not examine whether this regime increased the numbers of pregnancies achieved. Tobacco smoking appears to reduce sperm motility and should be discouraged, as should excessive alcohol consumption which also has an adverse effect on sperm production. Anecdotal case reports suggest some benefit in terms of fertility from these measures, which are at least free from side-effects.

Supplements of vitamin C (1g q.d.s.), vitamin E (100mg t.d.s.) and Zinc have been suggested on theoretical grounds⁶ but none has been reported to improve pregnancy rates.

The use of Mesterolone (Pro-Viron) was initially thought to improve semen quality⁸, but this impression has not been confirmed by later studies⁹. As its use does not increase pregnancy rates it should no longer be prescribed.

Artificial insemination of the male's semen into the cervical canal (AIH) is often performed but unless the cause of the subfertility is related to mechanical problems with semen deposition on the cervix, it does not improve pregnancy rates. Hence its use should be restricted to couples with these particular problems.

COUNSELLING

In some cases it is obvious from the outset that the chances of the couple achieving a pregnancy are remote. The GP's role here is often vital in helping them face and accept their childlessness¹⁰. This childlessness is a life crisis experienced as bereavement, but with no specific focus for the grief¹¹. This often leads to depression which needs to be recognised and correctly treated.

Self-help groups have become common as many couples feel their doctors and the NHS have no time or interest in their problem. **Issue**, the National Fertility Association, is the largest and produces a number of information sheets as well as holding meetings and organising local support groups. This year it is promoting a National Fertility Week (8 – 15 May).

CONCLUSION

The initial investigation and management of subfertility is quite simple and within the remit of any GP.

If testing of tubal patency by HSG was available to GPs then the role of the hospital specialist could be confined to more complex investigations and treatments, with a reduction in the waiting time for patients.

Care of the couple does not cease with a final diagnosis – for some, the problem is only just beginning.

Issue, The National Fertility Association, St. George's Rectory, Tower Street, Birmingham B19 3UY (Tel: 021-359-4887).

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L E E S E B E Q U E S T

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