

## FACTSHEET

### UNEXPLAINED INFERTILITY

It can feel very unsatisfactory to be given a diagnosis of unexplained infertility, and couples often wonder whether more detailed tests might produce some kind of answer. The reality is that some people who have no apparent medical problems still do not get pregnant. Studies have shown that even in this group, over a period of seven years, 36% will eventually conceive, and over the same period, in a similar group who cannot conceive again after having one or more children, 79% will eventually conceive. Some fertility problems just reflect this inefficient human reproduction. One study of unexplained infertility of less than two years duration showed that 50% of these couples would conceive over the next two years, and suggested that the right treatment was to do nothing.

#### What is unexplained infertility?

Infertility may be said to be “unexplained” if the woman is ovulating regularly, has open fallopian tubes with no adhesions, fibrous growths or endometriosis and if the man has normal sperm. Intercourse must take place frequently, at least twice a week, particularly around the time of ovulation, and the couple must have been trying to conceive for the previous two years at least.

Using these criteria, about 10% of all infertile couples have unexplained infertility according to the most often quoted figures. However, it is thought this figure could be lower if thorough screening is carried out. Some studies show around 28% of patients experiencing unexplained infertility, so a great deal has to do with how thoroughly diagnostic tests are performed.

#### Possible causes of unexplained infertility

##### 1. Anatomical abnormalities

It used to be thought that a retroverted uterus (or a tilted womb) was a cause of infertility, but this is no longer taken to be the case. The position of the cervix is unlikely to be so abnormal that sperm are unable to reach it. It is possible that there may be failures in the mechanism in the mouth of the fallopian tubes which allows them to pick up the egg. Abnormal levels of hormones called prostaglandins, which are responsible for making the muscles contract, may interfere with the passage of the egg in the tube. High prostaglandin levels, however, are usually associated with endometriosis, and this condition is likely to be detected. Scar tissue, often associated with inflammation of the womb lining, or large multiple fibroids can interfere with the process of reproduction by making the womb unreceptive to a fertilised egg. Scar tissue can also result in damage to the fallopian tubes.

To aid accurate diagnosis of the cause of infertility, investigations should include vaginal ultrasound scans and hysteroscopy. Vaginal ultrasound will pick up abnormalities within the womb and abnormalities with the ovaries, which would otherwise be missed by a laparoscopy. If vaginal ultrasound is not available, a hysteroscopy should be performed at the same time as a laparoscopy so that any problems within the womb, which could cause infertility, may be excluded.

##### 2. Abnormal development of the follicle and of ovulation

In some women the egg may be released from the follicle in which it develops before it is properly mature or it may not be released at all leading to the formation of a cyst (see point 4).

### 3. Abnormal eggs

It would appear that a very small number of cases of unexplained infertility are due to the persistent production of abnormal eggs. These may have a deformed structure or chromosomal abnormalities.

### 4. Trapped eggs

In some cases it would appear that eggs are produced, and mature correctly within the follicle. This goes on to become a "corpus luteum" (the next stage of development) but without first bursting to releasing the egg. The egg is therefore effectively "trapped" inside the unbroken "corpus luteum".

### 5. Luteal phase abnormalities

This is perhaps the most important of all causes of "unexplained" infertility. This is where the part of the cycle that follows after the egg has been released from the ovary, is abnormal in some way.

After releasing the egg, the follicle which contained it in the ovary goes on to become the "corpus luteum" (this translates from the Latin as "yellow body"). The corpus luteum produces the hormone called progesterone. Progesterone is essential for preparing the lining of the womb to receive the fertilised egg, and for sustaining the embryo in its first seven weeks of life.

Several things can go wrong with progesterone production: the rise in output can be too slow, the level can be too low, or the length of time over which it is produced can be too short. Problems during this phase of the cycle are known as "luteal phase defects", and can be investigated either by carefully examining samples from the lining of the womb (endometrial biopsy) or by monitoring the progesterone output by taking a number of blood samples on different days after ovulation so that the progesterone level in them can be measured. Problems in the luteal phase may also occur as a result of abnormal levels of the hormone prolactin.

#### Treatment

Problems in the luteal phase seem to relate to levels of the hormone follicle stimulating hormone (FSH) and luteinising hormone (LH). If the levels of FSH are not right this can be responsible for lower levels of progesterone being produced by the corpus luteum. Low LH levels can also be responsible for failure to develop an adequate secretion of progesterone. The ratio between LH and FSH appears to be critical to progesterone production.

For these reasons treatment with the drug, clomiphene may be useful in helping to restore adequate secretion of FSH and LH. Luteal phase abnormalities, abnormalities in the development of the follicle and in the timing of ovulation can thus be helped.

Direct treatment with progesterone can also help luteal phase abnormalities. The progesterone can be given either as injections or vaginal suppositories. Synthetic "progestin" should not be used as they have an anti-progesterone activity, and furthermore, they become broken down into male hormones within the body; this could adversely affect the developing embryo.

Of the other possible causes of "unexplained" infertility, not all are treatable with our current state of knowledge.

Undoubtedly as our knowledge increases and our techniques and treatments improve the diagnosis, "unexplained infertility" will become less and less frequent. No-one should expect that all these factors will automatically be taken into account when they are told that the reasons for their infertility are inexplicable, and a little gentle prodding or some pertinent questions may be helpful.

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