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Fact Sheet 43

Unexplained infertility

Updated Mar 2014

Infertility is a difficult and stressful situation to deal with at any time in a couple's life, but being told there is no identifiable cause for the delay in achieving a pregnancy can be a devastating blow for some. A diagnosis on 'unexplained infertility' is given to approximately 15% of couples with infertility.

Achieving a pregnancy is a very complicated process and depends on many factors. Eggs and sperm (the gametes) must both be present and of 'good enough' quality. There needs to be no obstruction to the gametes meeting (i.e. healthy fallopian tubes). Fertilisation must occur and a genetically normal embryo be created. The embryo must then implant into a normal endometrial environment (lining of the womb) in the uterus and start to develop.

Even in a perfect situation - the chance of achieving a pregnancy on a single cycle is around 15-25% depending on age of the woman.

85% of couples that are not avoiding a pregnancy, and having regular unprotected intercourse, will be pregnant within 12 months. Within the following 12 months, half of the remaining couples will achieve a pregnancy, giving a total of 95% of couples will have success within 24 months. This is an important statistic, as many couples feel they have not 'tried' for a pregnancy unless they have actively tracked ovulation. A woman under 35 is considered infertile is she fails to become pregnant in 12 months. For a woman over 35, investigation should begin once six months has passed without success.

While we refer to 'infertility', the reality is that most couples are in fact 'sub-fertile' (infertile suggests that there is no chance that the couple will conceive without treatment - an example of this is a man without sperm in his ejaculate, or a woman without a uterus). Sub-fertility may have multiple mild issues instead of a single 'major' factor e.g., the presence of a minor sperm issue plus irregular ovulation.

The issue with a diagnosis of 'unexplained infertility' is that there may be a reason - it just hasn't been identified as yet. So how much investigation is required to comfortably label a couple with the diagnosis of 'unexplained infertility', and what can we do to help these couples? Many couples falling into the 'unexplained' group will in fact have a number of very mild factors affecting their chances.

Investigations

The diagnosis of 'unexplained infertility' is a diagnosis of exclusion. This diagnosis can only be made after comprehensive investigation of the woman and her partner. It is generally agreed that, at the least, we must confirm that eggs are being released (confirm ovulation), that fallopian tubes are not blocked and that sperm are present with reasonable parameters (number, motility and morphology).

Oocytes (eggs).

Blood progesterone levels can confirm ovulation. Blood is collected about 1 week after ovulation is thought to have occurred. This is confirmed by an increased progesterone level. AMH (Anti-Mullerian Hormone) is also commonly being ordered in blood testing now. It is an indicator of ovarian 'reserve' rather than 'function'. On the whole, it is a poor indicator of chance of pregnancy, a woman's age remains the best single predictor for this.

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Tubal Testing.

There are two main methods to assess tubal 'function'. The first is an outpatient method utilising X-ray or ultrasound, most commonly hysterosalpingogram (HSG) - flushing radio-opaque dye through the cervix, uterus and tubes. The second option to assess tubal patency is a laparoscopy (keyhole surgery) to visualise the pelvis and flush the tubes at the time.

A major benefit of a laparoscopy is that the doctor is able to identify endometriosis which may be present in up to 30% of 'unexplained infertility', and to exclude abnormalities of the genital tract. If endometriosis is treated, this can significantly improve chance of pregnancy. The risks of the procedure need to be weighed against this information.

Sperm parameters.

There is enormous variation in semen parameters between fertile men, and also between specimens from the same man over a period of time. Classically, semen analysis has measured 3 parameters - number of sperm (in millions per ml of semen); motility (percentage of sperm moving rapidly, slowly or immotile); and morphology (percentage of 'normal' looking sperm).

These investigations cover the basic requirements to achieve a pregnancy. But if only investigating these issues, there is a chance of missing information that would convert a couple with 'unexplained' infertility to that with a known cause.

Age of couple.

The woman's age is a very important factor in determining the baseline chance of pregnancy for a couple. While more prompt investigations occur if a woman is over 35 years old, the reality is that the chance of pregnancy per month in this population is lower than in younger women (and in fact it should take longer for a couple to conceive) The reason we investigate and treat earlier in this group is that we don't have the luxury of time in which to find treatable causes for infertility. We should identify treatable causes sooner, and move on to maximising a couple's chance of conception.

More and more data is also showing us that the age of the male partner also plays a big part in the likelihood of pregnancy as well as in the chance of miscarriage. There is information regarding the damage that occurs to sperm while they are being stored within the scrotum waiting to be ejaculated (on average for around 3 months). This level of damage is increased as men age towards, and past, 38 years and with smoking' obesity; chronic disease, operations involving scrotum or testes, variations in anatomy within the scrotum such as varicocoeles (varicose veins in the scrotum) and hydrocoeles (fluid filled spaces in the scrotum). A routine semen analysis does not provide this information.

Other investigations that may shed more light on a potential reason to explain a couple's infertility are listed below - along with some areas of advice for our patients.

- Karyotype - assessing chromosomes of both male and female
- Thyroid function and antibodies
- Vitamin D levels
- Glucose testing for undiagnosed diabetes or impaired glucose tolerance
- Cervical factors or sexual dysfunction
- Measuring DNA fragmentation in the sperm
- Tests attempting to look for 'implantation failure' - this is a very grey area at present. Testing comprises of a number of as yet unproven investigations, and importantly, these investigations can lead to unproven treatments being suggested.
- The importance of both parties being as fit and healthy as possible, to maximise chance of pregnancy, and to minimise chance of complications within a pregnancy in the future.
- Identifying the presence of fibroids or endometriosis in pelvis
- Promoting healthy eating/exercise and aiming for BMI less that 25 - this will improve the baseline chance for the couple.

Psychological stress

Couples are very often significantly stressed when they meet a fertility specialist. There is a general feeling that stress is the cause of the infertility, and this misconception is widely supported in the community of well-wishers. It is not uncommon that couples, especially the female partner, are advised by friends and relatives to 'relax' and it will happen. It is more often the case that the infertility is the cause of psychological stressors, and not the other way around.

There is no evidence that stress within a treatment cycle has any impact on the outcome of treatment. Couples stressors and expectations must be managed as part of the big picture. Psychological counselling will be easily accessible to women and their partners through their fertility units, and they should be encouraged to make use of these service.

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How to treat unexplained fertility

So what can science offer couples with unexplained infertility? Couples with unexplained infertility make up an important and substantial proportion of many fertility units. The good news is that, even without a definitive diagnosis, reproductive technologies can help - and in many cases have very good results.

Ovulation tracking and timed sexual intercourse.

While this sounds a very basic intervention, many pregnancies are achieved simply by tracking a woman's cycle with bloods and or ultrasound. This allows the couple to gain a working understanding of the menstrual cycle, and for them to maximise their chance of natural conception.

Ovulation induction

Research tells us there is no good place for ovulation induction without insemination for treatment of unexplained fertility. If a woman is already ovulating, some of the drugs may indeed have a detrimental affect on pregnancy (anti-oestrogen effects of clomiphene citrate).

Intrauterine insemination (either with or without Ovulation induction)

This too is about maximising chance of pregnancy, by tracking ovulation with bloods and ultrasound scan in order to coordinate a washed specimen of sperm to be 'inseminated' through the cervix and up into the uterus. This is a straightforward procedure. Pregnancy rates are quoted at similar to those in nature when a couple first starts trying - around 15%. Most evidence suggests that if a couple is going to get pregnant using IUI, they will do so within the first 2-3 cycles. If ovulation induction is also used, patients should be aware of risk of multiple pregnancy of 5-10%.

In-vitro fertilisation

IVF gives the scientists and clinicians the most information about the basic building blocks required to achieve a pregnancy. Assessment of oocyte (egg) quality, sperm quality and eventually embryo quality can often give a hint as to where the issue may be. IVF pregnancy success rates in couples with unexplained infertility are at least as good as those seen in many other forms of infertility.

Dr Simone Campbell

Emotional factors: Unexplained fertility

It has been said that unexplained infertility is the most difficult to come to terms with emotionally. That "out of control" feeling associated with "infertility" is exacerbated by the repeated trauma of invasive investigation which reap no reward.

Sometimes couples start to wonder if there is some underlying mental health factor preventing conception and this is often reinforced by well-meaning friends suggesting they should just "relax" or "take a holiday". As a result the course is set for self doubts and there is a temptation to find a release by blaming a past event or blaming your partner.

However the reality of this situation is the same as for any other diagnosis of infertility. As individuals and as a couple, you are experiencing a grief reaction. It is heightened by the fact that there is nothing tangible to focus your grief upon. It is more difficult to resolve when intellectually there is no reason for this event.

Coping strategies

- Research the problem. Read and learn as much as possible. Talk to several professionals and consumers. Make lists of questions.
- Keep communication lines open with your partner. You will need to talk about things regularly and you may have different needs at different times. Be patient with each other.
- Allow for times of anxiety and sadness.
- Allow yourself private times.
- Try extending the support network by sharing with family and friends.
- Consider reducing other stressful activities and maybe restructure other commitments when it becomes overwhelming.
- Remember you don't have to go it alone even though that feeling of isolation can be haunting. There are professionals and self-help groups out there but you need to let them help you.

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Supported by an untied educational grant from:

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