



Practice Points

- Take a full history to access menstrual cycle/ovulation.
- Arrange a sperm analysis to check for male involvement.
- Advise that not all couples need IVF.
- Refer to a fertility specialist early, especially if the female is older.
- Success depends on the woman's age.
- Success of egg freezing tends to be over-estimated in the media.

Investigating subfertility



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Developments in assisted reproductive technology mean more successes.

ABOUT one in six couples experience subfertility in Australia, so offering advice on assisted reproductive technology (ART) is an expectation in general practice. According to the BEACH program, between April 2007 and March 2012 there was one fertility/subfertility problem managed for 652 patient encounters. Referrals to specialists were at a rate of 49.8 per 100 female fertility/subfertility problems, and 15.9% were referred directly to an IVF clinic. The use of technology in conception has become commonplace: more than 5.5 million babies worldwide have been born thanks to IVF in the past 30 years.

It is never too early to refer a couple for specialist advice. A

sensible fertility specialist will tailor the investigations depending on patient age, priorities and history. For instance, a woman who is having difficulty conceiving and does not have cycles needs to be referred immediately. She probably won't need IVF but ovulation regulation/stimulation is cheap, easy, has low complications and a high success rates. A full history will be taken to assess the menstrual cycle and investigate underlying reasons for subfertility.

Subfertility is defined as the inability to conceive within 12 months of unprotected sexual intercourse but, if there is an obvious cause or the woman is older, investigate earlier. Failure to ovulate, endometriosis, PCOS, adhesions, fibroids and poor timing of intercourse/other pathologies may be the cause.

MEDICAL WORK-UP

Standard work up for subfertile couples may be as follows:

Females: blood test in first week of cycle (days two to four): luteinizing hormone (LH), follicle stimulating hormone (FSH), oestradiol, thyroid stimulating hormone (TSH), anti-Mullerian hormone (AMH). Day 21: blood test for progesterone. Immunity to varicella and rubella should be

checked. A pelvic ultrasound, performed by a gynaecological specialist, should be done as a work up if IVF is anticipated.

In this case, antral follicle count (AFC) will be done, alongside scanning for physical abnormalities, polyps, fibroids, ovarian cysts and to note position and ease of access to ovaries.

Males: Semen analysis to assess sperm motility, morphology, vitality, count and presence of anti-sperm antibodies will be arranged.

The couple can then be advised of results and options discussed at follow-up appointment.

WHAT'S NEW IN IVF

IVF is always undergoing small changes, resulting in ever-increasing success rates. The greatest change is the use of single embryo transfer (SET), which significantly reduces multiple pregnancy rates. Australia and New Zealand now lead the world with multiple pregnancy rates of about 6%. Stimulation is much simpler with the use of ELONVA, a seven-day depot injection, and monitoring has been minimised so that 80% of women get by with one scan and one blood test.

Ovarian hyper-stimulation syndrome (OHSS) has virtually been eliminated with the use of

GnRH antagonist stimulation cycles, GnRH agonist trigger and "freeze all" protocols if the woman has many follicles and no embryo is transferred in the fresh cycle.

The technology of pre-implantation genetic screening (PGS) is improving, and the cost is coming down. While PGS doesn't make any more normal embryos, it allows the elimination of aneuploidy (those that do not have 46 chromosomes) and saves transfer cycles that have no chance of succeeding because the embryo is abnormal. Egg freezing is much more successful with the vitrification technique. But the success rate is still grossly overestimated by proponents of social freezing.

Success depends on the woman's age: across the board about one in three embryo transfers result in pregnancy. In Australia, IVF is usually offered up to the ages of 45/46 using the women's eggs, and after this egg donation is advised. Half a woman's eggs are aneuploid at age 40. Success rates per embryo transfer at 40-plus decrease each year, at 40 maybe 20%, by 44 maybe 5% at best.

Depending on the situation, IVF has five steps, maybe six:

- Controlled ovarian hyper stimulation: Several different drugs and protocols, principally FSH,

are used to recruit multiple follicles. Ten to 15 is best; this usually lasts about two weeks.

- Monitoring: The follicular growth is assessed on ultrasound and hormone measurements are taken. This indicates how follicles are growing and the best time to collect mature eggs.
- Transvaginal ultrasound: Guided egg collection is undertaken in theatre under sedation. It is good to get about 10 oocytes.
- IVF: either the eggs are mixed with sperm or each egg is injected with a single sperm (ICSI) if sperm quality is poor, or the previous fertilisation rate is low. The embryos are then cultured, ideally for five days.
- Embryo Transfer (ET): the selected embryo is replaced transcervically using ultrasound guidance.
- Freezing: if there are embryos left that look strong enough to survive freezing and thawing, they are then frozen on day five or six as blastocysts.

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