## The SNOrtest

The IVF process is emotionally intense, physically draining and astonishingly expensive. But advanced medical knowledge and pioneering lab techniques are making the 'take-home baby rate' for women and couples better than ever, writes Danielle Barron

round 250 babies are born every minute around the world, and a growing proportion of these will have started life in a petri dish. Almost nine million babies worldwide have now been born thanks to in-vitro fertilisation, or IVF, and advances in medical knowledge as well as increasingly sophisticated laboratory techniques mean the assisted reproduction baby boom is set to continue.

millions of couples' prayers but, not surprisingly, it has its detractors. IVF is big business, and fears persist that the market model of assisted human to treatment options and decisions.

into IVF, or the offering of additional investigations and procedures that aren't medically necessary and may not increase your chances of success.

Professor Mary Wingfield is a consultant obste-trician and gynaecologist at the National Maternity Hospital at Holles Street in Dublin, and clinical director of the not-for-profit Merrion Fertility Clinic. She stresses that, first and foremost, the goal should be to optimise a couple's chances of conceiving naturally. "Undoubtedly, IVF is the best fertility treatment we have, but nature is better than IVF, The fertility industry has been the answer to so if someone can get pregnant naturally then that is much better," she says.

"We don't advocate rushing straight into IVF, but sometimes, particularly if the woman is a bit older, reproduction can muddy the waters when it comes that is the only logical way to go, as they might miss the boat. That can be a difficult balance with Criticisms levelled at fertility clinics include a patients' feelings, as sometimes someone will walk tendency to encourage couples to jump straight into the clinic, and perhaps the man has a very



Fertility treatment is the lowest of the low. A man will sometimes make it to the top of my list, and we can get the ball rolling, but in general they are forced into the private system

Helen Browne of the National Infertility Support and Information Group: 'I felt my feelings were worse than grief'

JOHN ALLEN

low sperm count, and straight away you know they are going to need IVF," she says, adding that couples can be "taken aback"

For a pregnancy to occur, four things must be in order, says Wingfield; the woman must be ovulating, the man must have sperm, they need to be having sex so the egg and the sperm can meet, and the woman's pelvis must be normal.

Point three is more of a problem than you might think. Wingfield says that a small but significant number of couples have problems with sex, and can benefit "hugely" from sex therapy.

If a woman has pelvic pathology – essentially, damaged fallopian tubes - the fertilised egg can't travel back up towards the uterus. According to the Endometriosis Association of Ireland, up to 50 per cent of women with infertility have endometriosis This condition, where the endometrial tissue that normally lines the womb also occurs outside it, can cause cysts on women's ovaries or adhesions in their pelvis. Adhesions or scarring in their pelvis from a previous infection such as chlamydia or from surgery can also be a major factor in infertility. In these instances, surgery is the first and often best option, says Wingfield.

"In vounger women we would recommend surgery first, but not very radical surgery, and you have to be careful that you don't damage the ovaries," she says, adding that it should be carried out by a specialist surgeon. "This is an important part of our work in terms of treating fertility.

But when all else fails, IVF is the only option. The good news is that there have been a number of incremental improvements in IVF over the years. which has seen the "take-home baby rate" soar from 10 per cent to 30 per cent on average, says Wingfield.

"It's much better than it used to be. If the woman is under 35, then with one treatment it is 50 per cent - you can compare that to couples with peak fertility who will only get pregnant every third time they try."

To get pregnant naturally, around 15 million healthy sperm are needed, but for IVF you need about 100,000. Of course, just one sperm and one egg make a baby, but understandably with an IVF cycle they like to maximise your chances.

For more common causes of poor sperm production and motility (the movement and swimming of the sperm), urologists have a range of strategies and interventions that can help improve sperm quantity and quality.

Supplementation can help, as can hormonal medication. Surgical intervention, such as sperm retrieval, may also be an option.

All of this is available in the public system, says

Ivor Cullen, a consultant urologist working at Unithat there are very few urologists trained in male reproduction and with funding constraints, cancer

a man will make it to the top of my list, and we can into the private system. Any man with an abnormal

in Ireland it has been managed by gynaecologists, which makes no sense.'

form of IVF where a single sperm is injected into an egg, has revolutionised the treatment of male factor infertility, but some men will simply have no sperm at all, a condition known as azoospermia Cullen received special training in groundbreaking urological procedures during his time in Britain and his endeavours to find sperm in men previously thought to be sterile are in serious demand.

A rare condition known as non-obstructive azo ospermia can benefit from an operation known as microsurgical testicular sperm extraction (micro-TESE), which can retrieve small numbers of immature sperm. This has been carried out more than 40 times in the past three years by Cullen and his team, in association with fertility providers, and there have been a number of successful pregnancies as a result. "For the right couple, this has been a

is the same for the couple. Wingfield outlines what a typical IVF cycle involves. "We try to get between ten and 15 eggs, and to achieve this the woman has to go on fertility drugs that she self-injects for ten to 15 days." The eggs are removed vaginally, and on the same day the man produces a sperm sample. The eggs and sperm are placed in culture, and by the following day, it will be obvious which eggs have been fertilised and are on their way to forming embryos. Three to five days later, all proceeding well, an embryo is selected to be put back into the woman's womb. Any extra viable embryos are frozen to be used in the future

Embryo transfer is a controversial topic with in the assisted reproduction field and thinking on the issue has changed dramatically in recent years. Transferring multiple embryos back into the womb may mean a multiple pregnancy, and this is now

high-risk pregnancies, and even twins carry much higher risk than normal pregnancies," Wingfield says, adding that when success rates were lower, more embryos were put back.

"One of the biggest side effects over the years with IVF were twin pregnancies, and now it's almost regarded as a failure if you get twins. It's much safer, if you've got two embryos, to put one back and freeze the other so you have two children two or three years apart.'

ab scientists may be hidden away in the dark, but they are providing that most critical of services - babysitting your precious embryos. What happens in the lab can make or break the success of an IVF cycle. Claire Moran is a clinical embryologist and the laboratory manager at Repromed Clinic in Dundrum. "The lab is open seven days a week," says Moran. "When people come in on Monday they don't realise I have been looking after their embryos all weekend."

Embryology is a rapidly developing field, and innovative lab techniques have contributed to the big leap in live birth rates. One of the biggest advances in IVE in the past decade is blastocyst culture, says Moran.

"We used to do our transfers on day two or three when it was still an embryo, but now it is routinely blastocyst transfer on day five. It gives a much better quality embryo because it is at the stage where it is just about to implant."

Blastocyst or embryo freezing techniques have also improved significantly. There's now a growing body of evidence to show that having a frozen em bryo transfer, where the embryo from a fresh cycle is frozen, to be implanted at a later date, is optimal.

"A lot of clinics in the US are moving towards a model where they no longer do any fresh transfers

- they simply freeze the embryos on day five, let the woman's hormones come back to normal, and then transfer the embryos during her next cycle, says Moran, adding that Repromed has been doing this since the beginning of 2019.

Claire Moran of the Repromed Clinic in Dundrum: 'The lah is onen seven days a week. When people come in on Monday, they don't realise I have been looking after their embryos all



Professor Mary Wingfield of the National Maternity Hospital in Holles Street in Dublin

"The thinking behind that is that you can manipulate the lining of the uterus a lot better in a frozen cycle, so now about 50 per cent of them are planned frozen transfers."

The clinic has painstakingly worked on perfecting the timing of embryo transfers, she says. "We are guite picky about when we do it – we check the woman's progesterone levels before we do their egg collection and we do a test called an embryo receptivity assay to determine the receptivity of the uterus, so we know when exactly we should place the embryos in there."

These measures have seen the clinical pregnancy rate - when a foetal heartbeat is detected by ultrasound - rise and rise.

"While the positive pregnancy test rate is about 70 per cent, our clinical pregnancy rate is now 50-55 per cent. This is huge, because even if you look at British or European statistics, that used to be around 25-30 per cent," says Moran.

The availability of time lapse incubation is another development that has had a definite impact. Being able to watch the embryo's development over time can let embryologists in on whether it is developing normally or not, allowing them to make a more informed decision on which embryos to select for transfer.

The ultimate embryo selection is PIGD, or pre-implantation genetic diagnosis. Historically developed as a means to prevent certain genetic diseases or disorders from being passed on, it is slowly becoming routine practice in IVF labs around the world.

"In the US, there are hardly any IVF cycles that hannen without it. The technology has come on so much that before you would check for about 28 conditions, but now we can sequence the entire genome of the embryo no problem," Moran says.

Repromed generally only offers the procedure to older patients or those who've had a number of failed cycles, but Moran believes it will soon become de rigueur. "It is invasive on the embryo itself, as you have to take cells directly from it, but I predict in the next few years we will be just doing it on every

embryo," she says. "In years to come, we will think back in amazement to the old days where we just used to transfer embryos without knowing their genetics.

Clinics where PIGD is routine practice would claim a 70 per cent live birth rate, but Moran says that it isn't routinely carried out enough in Britain or Ireland vet to obtain proper data.

Once the lab's work is done, the couple are once again dependent on mother nature. The notorious "two-week wait" to see if an embryo has implanted into the womb's lining is typically tense.

"That's usually a very difficult time for couples," says Wingfield.

If it works – halleluiah. If it doesn't, what next? If the first cycle isn't successful, couples with spare healthy frozen embryos can try another transfer with one of these. This process is significantly cheaper, at around €1,000 compared to €4,500 for a normal cycle of IVF. If they have no frozen embryos, however, the entire process must begin again.

There is no designated waiting time, but Wingfield says most couples will need a few weeks or even a few months to get over the disappointment of it not working

"People put so much into it, they do everything to be healthy, they stop smoking and drinking and are doing everything they can. They often need time to regroup. It varies – some people just want to get back in as quickly as they can, other people want to take a break and go on holiday, but medically in most cases you can start again very quickly."

Persistence will often pay off, but this may not be feasible, either emotionally or financially, Wingfield

"The treatment is very difficult, very emotionally and physically draining, and financially. If the woman is under 38 and if they can stick at it then most of them will get pregnant, but there is a big drop-out rate."

Helen Browne knows all about persistence. She founded the National Infertility Support and Information Group (NISIG) back in 1996 after her second failed IVF treatment. She says counselling - only offered by some fertility providers, and at an additional cost - helped, but she needed to speak to someone who truly understood her heartbreak.

"I had gone to counselling, but I felt I wanted to meet other people who had gone or were going through what I was going through. I felt my feelings were worse than grief," she says. Browne eventually had seven failed cycles and throughout this period continued to provide support for couples going through their own fertility journeys. Now the group runs regular support meetings, and Browne mans a 24-hour phoneline.

Peer-to-peer support can be a lifeline for people struggling with infertility, she says.

"People want to know that their emotions are normal. I see men in couples who think their wives are driven crazy, that they are obsessed, and then they come to our meetings and realise it isn't just her, it is everyone who is on the same journey. It's so hard for men, all they want to do is fix it, and they can't. Men need to be looked after too."

NISIG receives no public funding, and Browne admits continuing the badly needed service is often a struggle. But she says their support is essential for the hundreds of couples who contact them each week

"The clinics in Ireland do wonderful work: even in the absence of legislation, they carry it out under strict guidelines. But we are the people who pick

Human biology may dictate that we are all here to procreate, but the deep yearning for a baby is something that women experience on a whole other level, says Browne.

"As a little girl, what's the first toy you are given?" she asks. "A doll. You are placed in the caring role from the very beginning."

Part four of The Fertility Question will feature in the Magazine next Sunday, September 1



versity Hospital Waterford. "But the harsh reality is and life-threatening scenarios will always trump men with compromised fertility.

The public waiting list is 5,000, Cullen says. "Fertility treatment is the lowest of the low Sometimes get the ball rolling, but generally they are forced

semen analysis should see a urologist, but historically Intracytoplasmic sperm injection (ICSI), another

game-changer.

Whether it's ICSI or standard IVF, the procedure

considered a risk in itself

"Triplets and quadruplets in particular are very

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