Fit to Conceive

by SUE DUMAIS

Some fertility clients come to me for weight loss, while others just want to know what they should or shouldn't be doing in order to enhance their chances of conceiving. There is plenty of information and research available in terms of pre- and post-natal guidelines, but very little regarding fitness for fertility.

The Canadian Society for Exercise Physiology (CSEP) recommends accumulating 60 minutes of regular physical activity per day to stay healthy or to improve health. A regular exercise program can help you lose weight or maintain a healthy weight, increase energy, decrease stress, and increase self-esteem and overall well being.

So if regular physical activity offers so many health benefits, is it safe for women during conception?

According to Dr. Alice Domar, author of *Conquering Infertility* and founder of the acclaimed Mind-Body Fertility Program in Boston, vigorous exercise can:

- interfere with normal reproductive functioning
- elevate cortisol levels (the flight or fight hormone)
- cause women to stop ovulating and menstruating

High intensity exercise programs, such as "Boot Camp" classes at the gym, are highly motivating for participants and will whip them into shape, however, in some cases, this comes at a cost. After participating in vigorous fitness programs, some women experience menstrual irregularity or amenorrhea, where their menstrual cycle stops altogether.

What is considered vigorous exercise?

I would suggest using the perceived exertion scale and the "talk test" to assess the intensity level of your workout, and I encourage you to stay within the guidelines that follow.

Rate how hard you are working based on the following scale. I encourage you to stay somewhere between 3 and 4.

1. Perceived Exertion Scale.

1	Very Easy
2	Easy
3	Moderate
4	Somewhat Hard
5	Hard
6-9	Very Hard
10	Too Hard

2. Talk Test. If you can carry on a conversation while exercising, catching your breath between sentences, you are likely working at a moderate level of intensity. If you can't talk continuously or are gasping for air in between words you are working too hard. Make a point to check

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in frequently using this technique, so you can learn to assess your own intensity during and after exercising.

Fitness for fertility

Walking is great cardio exercise. A nice brisk walk can provide an adequate level of intensity to challenge your cardio vascular system while preserving your reproductive health. Talking a walk in nature can also feed your soul. Be mindful of your surroundings as you walk. Be aware of the trees, flowers, birds, insects and other animals. There is so much to explore. Practicing mindfulness during a walk can help slow your thoughts and reduce stress and anxiety. It is like meditation in movement.

A major concern I have when working with a fertility client is whether they are holding unnecessary tension in the pelvis and lower belly. Increased tension in the abdominal and pelvic muscles can negatively impact your fertility by reducing the nourishment to your uterine lining, creating a poor environment for implantation and pregnancy. Releasing the tension in your pelvis improves blood circulation and energy flow to your reproductive organs.

To do this, I suggest a combination of gentle deep core muscle isolation exercises to provide lower back and pelvic stability, and yoga poses to help open the pelvis and increase circulation. I would avoid high intensity abdominal exercises as this often leads to more tension. It is just as important to be able to contract the deep stabilizing muscles of your core as it is to be able to relax them. Some of my clients have difficulty releasing tension in this area. I call this condition being "stuck in the core." In this case, I would focus solely on yoga, deep tissue stretching and breath work to release these tense muscles.

Resistance training helps to increase muscle strength and endurance. For example, performing a squat will build strength in the muscles of your legs and buttocks. Resistance training is generally recommended 2-3 times a week. For fertility clients I recommend some form of resistance training 1-2 times a week. I also encourage my clients to train using their own body weight and mind-body awareness. You can make an exercise more challenging simply by creating the resistance, and using your mind to purposefully activate the muscles required to perform the movement. Through practicing mindfulness, exercises that seemed simple or easy become more challenging. This means you will see results faster, even when using a lower level of intensity. Mind-body awareness improves communication between the brain and central nervous system and improves how you move. You will begin to feel stronger performing everyday tasks. If you do decide to use hand-held weights or resistance machines, choose a lower weight and low repetitions (e.g. 8–10 repetitions per exercise at a low weight).

There is no one recipe for all. Everyone responds differently to exercise. Some women need to begin exercising while others need to slow down or stop altogether. Other factors to consider are whether weight loss or weight gain is needed. Obesity as well as being underweight can negatively impact fertility.

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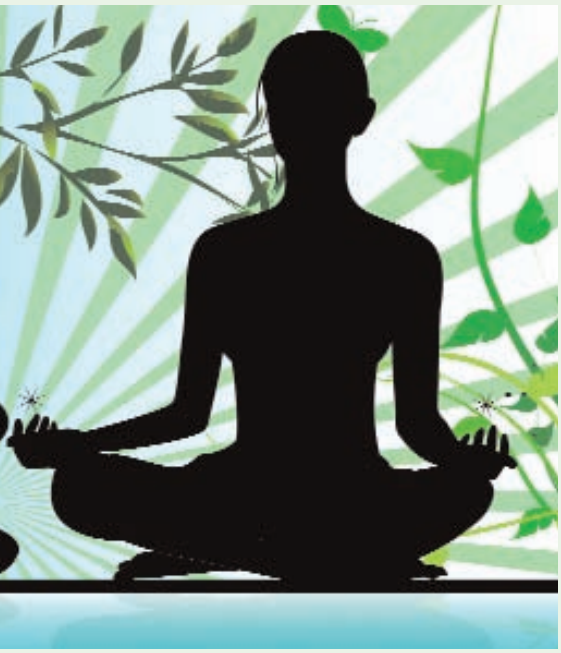

The question is, what do you need to do to become fit to conceive?

I have created some guidelines to help you.

1. Start slowly and build up to 30-60 minutes a day of regular physical activity (walking, swimming, yoga). This can be accumulated throughout the day.
2. Use the perceived exertion scale and the talk test to maintain a low to moderate intensity throughout.
3. If your menstrual cycle is irregular or has stopped, discontinue any high intensity exercise programs and consult your health care provider.
4. Find simple ways to be active (e.g., take the stairs instead of the elevator, park farther from your destination and walk).
5. Think outside the box—choose an activity you enjoy, like belly dancing.
6. Incorporate low intensity resistance training 1-2 times per week, focusing on mindfulness.
7. Practice gentle core stability exercises and avoid high intensity abdominal training.
8. Incorporate yoga and deep relaxation each day.
9. Make healthy food and lifestyle choices as often as you can.
10. For male fertility, I recommend avoiding long distance cycling, tight fitting or restrictive undergarments and overheating of the testicles.

Mindfulness

Your thoughts and beliefs play a big role in your success. If you hate your body or think you are lazy, you will have a hard time motivating yourself to reach your goals. Be aware of your thoughts about your body, your weight and about physical activity. Physical activity should be enjoyable. If you hate going to the gym or walking on a treadmill you are less likely to continue long term. Find something you enjoy! Consider registering for a group class, hiring a personal trainer, or exercising with a friend. When you make a financial commitment or have an appointment with someone, you will feel motivated to show up even on the days you are tired. Also group classes and personalized training can provide the variety and motivation many people need to stay on track with their fitness goals.

Focus on the benefits of moving your body in an enjoyable way. For example, I practice yoga every morning because it helps clear my mind and body, and improves my ability to focus all day long. Belly dancing allows me to shake off any stress or worries and I feel sexy and grounded when I dance. Notice how you feel before and after your physical activity. Be aware of the positive effects on your mind, body and soul. As you focus more on how a specific exercise helps you feel better, it becomes easier to make it part of your daily routine.

Come up with a statement or affirmation to remind you that staying or becoming physically active is important to you. For example, "I love to move my body because I feel more energetic and alive." Your body is an amazing system that is capable to taking you wherever you need to go. Instead of being frustrated with what is wrong with your body, focus on how your body is working and what your body can do for you. Accept your body exactly as it is in this moment. Acceptance doesn't mean you will have to live with it the rest of your life. It allows you to make peace with where you are. Embrace your physical body exactly as it is and begin to dissolve judgment and self-criticism: say, "I am where I am, and it is ok." Acceptance creates space for new supportive thoughts to keep you motivated.

If you are still unsure where to begin or how to modify your current exercise program, I recommend you consult a Certified Personal Trainer. Ideally, find one that specializes in fertility and/or pre- and post-natal health and fitness. They can help you set goals based on your specific needs. Be sure to let them know you want to conceive and that you would like to follow the fertility fitness guidelines outlined in this article. The most important thing to remember is that deep down, you know what is best for you. Follow your inner guidance or intuition. Make choices that are best for you and for your overall health, and you will be well on your way to being fit to conceive.

About the author

Sue Dumais' own struggles with fertility combined with her passion for yoga inspired her to co-found Family Passages Mind Body Fertility Studio in Vancouver, where women and couples can experience mind body programs, Yoga for Fertility and self-care designed to support them on their fertility journey. Sue has recently published a *Yoga for Fertility Handbook* and *A Strong Core for Life*. She has also developed several online audio classes and self-help programs as well as Fitness Fertility Specialist Certification and Yoga for Fertility Instructor Training courses. Sue can be reached at **604-266-6470** or visit **www.familypassages.ca**

Ressources

Fit to Conceive Audio Self Help Course, Sue Dumais

Fitness Fertility Specialist Certification Manual, by Sue Dumais

A Strong Core for Life, by Sue Dumais

Conquering Infertility, by Dr. Alice Domar & Alice Lesch Kelly

The Infertility Cure, by Randine Lewis

of fertility experts and spokespeople tends to bear it out. Before long, the story of the "octs" had ballooned into a full-blown ethical debate.

To many of our readers, it will come as no surprise that Nadya Suleman's octuplets were a result of assisted reproductive treatment. What may be more of a shock is that she already had six children—all born through IVF—when she got pregnant with the eight. According to Suleman's mother, Nadya had blocked fallopian tubes, and needed IVF to conceive. All of her children were conceived using donor sperm, and she had gone through ovarian stimulation and IVF several times previously.

When she became pregnant with eight babies, Nadya's doctors suggested embryonic reduction, an option that is commonly offered to women in multiple pregnancies. It entails removing one or more embryo to give the others a better chance of survival. Ms. Suleman refused, choosing instead to try for the whole eight.

"Anyone who transfers eight embryos should be arrested for malpractice," bioethicist Arthur Caplan of the University of Pennsylvania told ABC News. Current guidelines suggest transferring a maximum of one to four embryos, depending on the age of the mother—in women under 35, the implantation rate is quite high for fresh or frozen embryos. Nadya Suleman was 33. In a televised interview, Suleman announced that she had in fact had six embryos transferred; two of these presumably became sets of twins. Six embryos is still higher than the current recommended maximum, but Suleman explained that this was her last cycle of IVF, and that she had cryopreserved embryos remaining from previous cycles. She had them transferred because she did not feel right about destroying them.

Apparently, her motivation for having such a large family was her sheer love for children, but deliberately having so many at once was less than considerate to the babies themselves. Multiple births have serious and sometimes fatal consequences for mothers (most often gestational diabetes and pre-eclampsia) and for infants (prematurity with low birth weight, infant mortality, respiratory and intestinal problems, and cerebral palsy, among others). Even in the best-case scenario, where all the babies survive in good health, there are lifelong psychological implications for higher-order multiples. In the case of octuplets raised by a single parent, one can hardly imagine what they have to look forward to: it seems unlikely that any of these children will ever receive their mother's undivided attention.

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And then, of course, there's the matter of cost, starting with the well-publicized fact that 46 doctors were present at the caesarean delivery. If the average obstetrician in the US makes $230,000 per year, or around $110 per hour, we can estimate a cost of $5060 per hour in doctors' fees during the delivery alone. That does not include the cost of nurses and other staff, medical supplies, or the four delivery rooms that were reputedly needed for the births. One source estimated that the hospital bill by the time all the infants are discharged will likely approach one million, and this is before the usual baby costs kick in: diapers, clothes, food, cribs, car seats, strollers, home help—times eight.

So far, in spite of her reckless decision, Nadya Suleman and her octuplets have survived against the odds, and are now calling into question the ethical practice of multiple embryo transfer. Is it fair to endanger potential infants by transferring multiple embryos? Is it fair to impose the enormous cost of high-order multiple births on tax payers? Once it was discovered that Nadya Suleman was divorced, had no fixed income, and already had six children, public opinion turned strongly against her. Most women would not be able to afford the number of IVF cycles needed to have 14 children, and of those that could, it seems unlikely that many would risk their health or the health of their potential babies by having so many embryos transferred at such a young age.

It is unfortunate that what certainly seems to be a very unique case should draw so much attention to the issues surrounding IVF-related multiple births. Nadya Suleman's decision to transfer so many embryos and to carry octuplets to term has made her a hero to some members of the right to life movement, although in fact, her chances of losing eight babies were far greater than her chances of having any born alive. We can understand, even applaud Suleman's unwillingness to destroy the embryos that represent potential pregnancy and childbirth. But there are other possible solutions to this dilemma than aiming for a high order multiple pregnancy. By donating her embryos to another would-be mother, Suleman could have satisfied her conscience that her embryos were going to a good home, and given someone else a chance at the same time. After all, she's been the recipient of donor gametes herself. The ethical choice in this situation would have been for Suleman to give back to the community.

The one benefit this case may bring to the world of infertility treatment is to

raise awareness of the lack of funding for IVF treatment, and the effect this has in particular on the rate of multiple birth. Across Canada, there is currently very little healthcare coverage for IVF treatment; most provinces have no coverage at all. Patients pay out of their own pockets for a difficult and risky process, and understandably, they often choose to have multiple embryos transferred in the hope of increasing their chances of pregnancy.

As long as the government refuses to provide coverage for IVF, infertility will remain a fringe health issue. If the government were to provide coverage, it would be in a better position to monitor the number of embryos transferred. According to a recent financial analysis, full reimbursement of IVF treatment in Canada would result in 50% fewer multiple birth pregnancies, 40% fewer twins, 88% fewer triplets, and 3500 fewer low birth weight babies over a five-year period. This would protect fertility patients and infants from the heath risks of multiple pregnancies, and it would also protect taxpayers from assuming the enormous cost of the latter.

Of course, there is no question at the moment of the government of California initiating health coverage at all, let alone a program for IVF funding. But the story of Nadya Suleman's octuplets is a larger-than-life illustration of the issue of IVF and multiple births. It is to be hoped that legislating bodies worldwide will take notice, and recognize in IVF yet another area of healthcare in need of support.

About the author

Naomi Louder is a writer, editor and translator from Montreal. She has edited Creating Families on a contractual basis since February 2008.

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IN VITRO MATURATION (IVM)

by WILLIAM M. BUCKETT, MB, ChB, MD, FRCOG

What is IVM?

In the last four decades, since the birth of the first child conceived as a result of *in vitro* fertilization (IVF) and embryo transfer,[1] there has been an explosion of interest in assisted conception and in the practice of IVF particularly. IVF is now performed in nearly every country of the world and hundreds of thousands of babies have been born worldwide.

Most IVF protocols use drugs to effect ovarian stimulation and therefore enable a large number of mature oocytes (eggs) to be collected. This in turn allows more embryos to be generated and transferred, thereby resulting in higher pregnancy rates[2] and the possibility of freezing extra embryos and using them at a later stage (such as after the birth of a baby).[3]

However, there are several potential problems with ovarian stimulation - the drugs are often costly and there is an increased the need for blood and ultrasound monitoring.

Ovarian hyperstimulation syndrome (OHSS) is the most serious complication of ovarian stimulation and IVF[4] and can only be completely prevented by avoiding ovarian stimulation altogether.[5]

IVM is the collection of immature oocytes from ovaries which have not undergone any stimulation with drugs, their subsequent maturation *in vitro* (IVM) to mature oocytes capable of being fertilized with sperm (See Figure 1), and ultimately the transfer of these embryos into the uterus where there has been appropriate synchronization of the endometrium.[6]

Natural cycle IVF – where a single mature oocyte is collected – has been used, with varying degrees of success, for women who need to avoid the risks and side-effects of ovarian stimulation[7, 8] although the success rates *per cycle* are low. However, during the follicular phase or early part of the menstrual cycle,

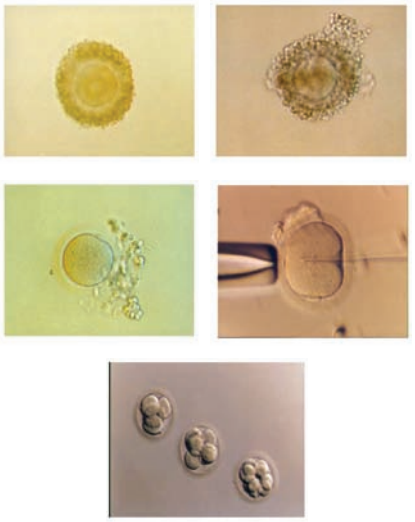


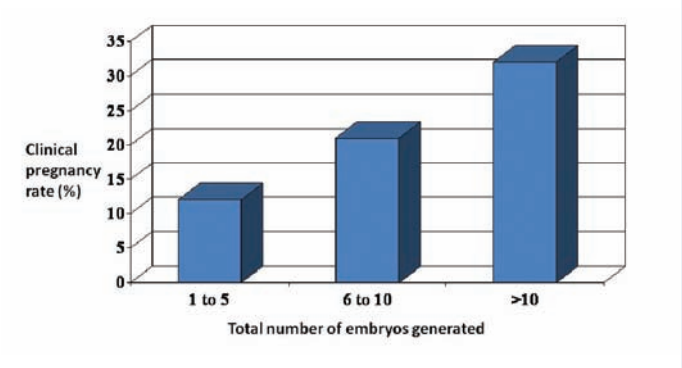
Figure 1. The maturation in vitro of an immature oocyte through ICSI to embryos for transfer.

within the cohort of antral follicles from which a single dominant follicle develops, there are also many immature oocytes.[9] The ability to collect these immature oocytes and effect their maturation *in vitro* allows the generation of multiple embryos, [10,11,12] which therefore provides similar benefits to conventional IVF, while avoiding the problems associated with ovarian stimulation.

So, IVM is a modification of IVF where ovarian stimulation is avoided yet multiple oocytes can still be collected.

Who should consider IVM?

Clinical pregnancy and live birth rates following IVM are highest in women with polycystic ovaries (PCO) or polycystic ovary syndrome (PCOS). Therefore women with PCOS, ultrasound-only PCO, or a combined antral follicle count of greater than 20 who need IVF are the best candidates for IVM. The antral follicle count is the best clinical predictor of the number of immature oocytes that may be retrieved and the best predictor of clinical pregnancy. (See Figure 2).[11]



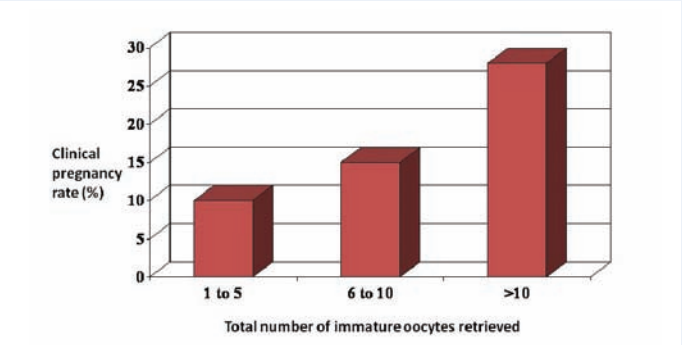


Figure 2. The relationship of (a) embryos generated, (b) immature oocytes retrieved, and (c) number of antral follicles to success following IVM

Incidently, these women are also at increased risk of ovarian hyperstimulation syndrome (OHSS) and therefore would benefit most from avoiding ovarian stimulation, as well as having the highest success rates with IVM.

Certainly IVM should be considered in any woman who needs IVF and is at high risk of OHSS or who has had cycles repeatedly cancelled because of the risk of OHSS.

Furthermore, IVM is also indicated in women who need to avoid ovarian stimulation – particularly those at risk from high estrogen levels. Examples would include women undergoing fertility preservation with breast cancer,[13] survivors of estrogen dependent tumours, or women with servere thrombophilias.

Finally, IVM has been used for oocyte donors who wish to avoid the risks and side-effects of ovarian stimulation.[14,15]

The history of IVM

The first successful IVM birth was in Korea. In this case immature oocytes were collected at cesarean section for oocyte donation.[16] Following this, the first pregnancy in a woman with anovulatory infertility using her own immature oocytes was reported in Australia[17] and a further pregnancy in a woman with PCOS was reported by the same group, using IVM combined with intracytoplasmic sperm injection, assisted hatching and blastocyst culture.[18] As women with PCO or PCOS undergoing IVF have an increased risk of OHSS from gonadotropins compared to women with normal ovaries, these women were an obvious group who may benefit from IVM and thereby avoid ovarian stimulation. Initial studies indicated that although immature oocytes recovered from unstimulated patients with PCO or PCOS can be matured, fertilized and developed in vitro, the implantation rate of these cleaved embryos was disappointingly low.[19,20,21] However, experience during the late 1990s and early 2000s indicate that IVM using FSH or hCG priming before immature oocyte retrieval, leads to clinical pregnancy and implantation rates of 30-35% and 10-15% respectively.[22] Further studies and current data show that pregnancy rates of 30-40% are achieved in women with the higher numbers of antral follicles associated with PCO or PCOS.[23]

IVM is now performed throughout the world with centers in Europe (primarily France, Italy, the Scandinavian countries, and the United Kingdom) and the Far East (Japan, China, Taiwan, Korea, and Vietnam), as well as in Canada and the United States.

IVM procedure

The steps involved in clinical IVM cycles are:
(i) cycle initiation
(ii) immature oocyte retrieval
(iii) in vitro oocyte maturation
(iv) fertilization
(v) embryo transfer
(vi) endometrial preparation and luteal support

Cycle initiation
In women with absent or very irregular menstruation, the treatment cycle is initiated by the administration of oral, intravaginal, or intramuscular progesterone and the timing of the start of treatment can be planned. Withdrawal bleeding usually occurs within 3 days after the last dose. On day 2 - 4 following the onset of menstrual bleeding, a baseline ultrasound scan is performed to ensure that there are no ovarian cysts. Women with spontaneous or regular menstruation should have the baseline ultrasound when their menstruation starts.

Transvaginal ultrasound scans should be repeated on day 7 - 9 to plan the immature oocyte retrieval. In women with ovulatory cycles this should be performed before day 9-11 of the cycle and in women with anovulatory (irregular) cycles the retrieval can be performed on day 10 - 14 of the cycle. Prior to immature oocyte retrieval, women are primed with 10 000 IU hCG subcutaneously 38 hours before oocyte retrieval.

Immature oocyte retrieval
Transvaginal ultrasound-guided oocyte collection is similar to IVF – except the follicles are much smaller (See Figure 3). Aspiration of all small follicles is performed under IV sedation with para-cervical block or under spinal or general anaesthesia. A multiple puncture technique is used. The collection needle should flushed regularly to prevent blockage with debris or blood clots. All aspirates are then examined under the microscope for cumulus-oocyte complexes comtaining the immature oocytes.

In vitro oocyte maturation
Following oocyte collection, the oocytes are evaluated and the immature oocytes are then transferred into the maturation medium for culture. The maturing oocytes are checked regularly for up to 48 hours.

Figure 3

a). Ovary during IVM collection with small, unstimulated antral follicles

b). Ovary during conventional IVF collection showing large stimulated follicles

Fertilization
Oocytes which are mature at the time of checking are then stripped and sperm are injected (as for ICSI). Fertilization is assessed 18 hours after ICSI for the appearance of two distinct pronuclei and two polar bodies. Sperm injection is used as the maturation process makes spontaneous fertilization harder.

Embryo transfer
Because implantation rates are lower with IVM, compared with ovarian stimulation and conventional IVF, often more embryos are transferred with IVM than would be transferred for conventional IVF in the same age group. Since oocytes are not necessarily mature and inseminated at the same time following maturation in culture, the developmental stages of embryos may be variable both within and between patients. Before transfer, all embryos for each patient are pooled and the best selected for transfer. Embryo transfer technique is the same as that employed for conventional IVF.

Endometrial preparation and luteal support
For the preparation of the endometrium, oral estrogen is given at a dosage depending on the endometrial thickness on the day of oocyte retrieval in divided doses, starting on the day of the immature oocyte retrieval. This is to synchronize the endometrium. If the endometrial thickness on the day of oocyte retrieval is thin, a higher dose is administered.

Luteal/progesterone support is started on the day that oocyte maturation is achieved and ICSI is performed and is the same as for conventional IVF. This is usually either intravaginal progesterone or intramuscular progesterone.

Disadvantages of IVM

Increased clinic/laboratory cost
IVM represents a significant reduction in the cost of IVF to the couple seeking treatment by virtue of avoiding the costs of ovarian stimulation - these can be significant, particularly when the GnRH-analogue long protocols are used either with or without recombinant gonadotrophins typically ranging from $2,000-$2,500 per cycle started. However, there are increased laboratory

costs. These include the direct and indirect costs of oocyte maturation, ICSI, and often assisted hatching. As the immature oocytes need to be checked every 12 hours, this also increases laboratory personel costs.

Lack of outcome data

The successful establishment of effective IVM programs for the treatment of infertility is still relatively new. Therefore the number of babies born worldwide is still relatively small at several thousand.

In brief, IVM is a modification of IVF where ovarian stimulation is avoided, yet multiple oocytes can still be collected.

Finally, there is a need for training - both for clinicians to learn the immature oocyte retrieval, which may be technically more demanding than conventional IVF because the follicles are smaller and the ovaries are often more mobile, as well as for embryologists to learn the maturation techniques.

Lower success rates

At present, many centers report clinical pregnancy rates following conventional IVF in excess of 40% per oocyte retrieval. [24,25] Although, some IVM programs reports success rates approaching this,[26] many do not. The only study to have tried to compare IVM with conventional IVF was a case matched controlled study of women with PCO or PCOS. This showed clinical pregnancy rates of 38% with conventional IVF and 26% with IVM,[27] although obviously there were no cases of OHSS in the IVM group.

Furthermore, miscarriage rates appear to be higher following IVM compared with conventional IVF – although the reasons for this are unclear.[28]

All centers which perform conventional IVF as well as IVM report higher clinical pregnancy and implantation rates with conventional IVF. The reduced costs to the couple, monitoring, and risks associated with IVM still make this treatment an attractive alternative to conventional IVF with ovarian stimulation.

All the studies so far have shown no increase in the obstetric, perinatal, and neonatal outcomes in women who conceived following IVM.[29,30]

Nevertheless, caution and appropriate counselling is needed regarding the unknown long-term effects of IVM on any children conceived as a result of treatment and continued follow-up is advised.

Conclusions

IVM has been shown to be an effective treatment for infertility in women with PCO or PCOS who need IVF for other indications and thousands of healthy babies have been born worldwide following this treatment.

IVM avoids the costs, monitoring, and risks associated with ovarian stimulation. This makes it an attractive treatment option not only for many women undergoing treatment themselves, but also for women wishing to donate oocytes.

IVM followed by oocyte or embryo cryopreservation is also an appropriate treatment option for women wishing to preserve their fertility – particularly those with estrogen sensitive tumours, such as breast cancer – prior to potentially sterilizing cheometherapy or radiotherapy. Although IVM is a relatively new treatment, early evidence from in vitro studies and from pregnancy outcome studies suggest that there is unlikely to be significant risk associated with this treatment.

About the author

Dr. William Buckett is Attending Physician and Sub specialist in Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, at the Royal Victoria Hospital, McGill University Health Centre, in Montreal, Quebec, Canada. He is also Assistant Professor in the Department of Obstetrics and Gynaecology, McGill University, Montreal.

References

1. Steptoe PC, Edwards RG. Birth after reimplantation of a human embryo. Lancet 1978; ii: 366.
2. Tan SL, Maconochie N, Doyle P, et al. Cumulative conception and live-birth rates after in vitro fertilization with and without the use of long, short, and ultrashort regimens of the gonadotropin-releasing hormone agonist buserelin. Am J Obstet Gynecol. 1994; 171: 513-20
3. Trounson A, Dawson K. Storage and disposal of embryos and gametes. Br Med J 1996; 313: 1-2.
4. Rizk B, Smitz J. Ovarian hyperstimulation syndrome after superovulation using GnRH antagonists for IVF and related procedures. Hum Reprod 1992; 7: 320-327.
5. Buckett WM, Chian RC, Tan SL. Can we eliminate severe ovarian hyperstimulation syndrome? Not completely. Hum Reprod 2005; 20: 2637.
6. Reinblatt SL, Buckett WM. In vitro maturation for patients with polycystic ovary syndrome. Semin Reprod Med 2008; 26: 121-126.
7. Claman P, Domingo M, Garner P, Leader A, Spence JE. Natural cycle in vitro fertilization - embryo transfer at the University of Ottawa: an inefficient therapy for tubal infertility. Fertil Steril 1993; 60: 298-302.
8. Nargund G, Waterstone J, Bland J, Phillips Z, Parsons J, CampbellS. Cumulative conception and live birth rates in natural (unstimulated) IVF cycles. Hum Reprod 2001; 16: 259-262.
9. Chian RC, Buckett WM, Tan SL. Pregnancy following natural cycle IVF combined with IVM: case report. Fertil Steril 2004; 82: 1675-1678.
10. Chian RC, Gulekli B, Buckett WM, Tan SL. Priming with human chorionic gonadotrophin before retrieval of immature oocytes in women with infertility due to polycystic ovary syndrome. N Engl J Med 1999; 341: 1624-1626.
11. Tan SL, Child TJ, Gulekli B. In vitro maturation and fertilization of oocytes from unstimulated ovaries: predicting the number of immature oocytes retrieved by early follicular phase ultasonography. Am J Obstet Gynecol 2002; 186: 684-689.

12. Buckett WM, Chian RC, Tanl SL. Human chorionic gonadotrophin for in vitro oocyte maturation: does it improve the endometrium or implantation? J Reprod Med 2004; 49: 93-98.
13. Rao GD, Chian RC, Son WS, Gilbert L, Tan SL. Fertility preservation in women undergoing cancer treatment. Lancet 2004; 363: 1829-1830.
14. Gulekli B, Child TJ, Chian RC, Tan SL. Immature oocytes from unstimulated polycystic ovaries: a new source of oocytes for donation. Reprod Technol 2001; 10: 295-297
15. Scharf E, Buckett WM, Chian RC, Sylvetsre C, Tan SL. Oocyte donation with IVM. Presented at ASRM Meeting, Philadelphia 2004.
16. Cha KY, Koo JJ, Ko JJ, Choi DH, Han SY, Yoon TK. Pregnancy after in vitro fertilization of human follicular oocytes collected from nonstimulated cycles, their culture in vitro and their transfer in an oocyte donation program. Fertil Steril 1991; 55: 109-113.
17. Trouson A, Wood C, Kausche A. In vitro maturation and fertilization and developmental competence of oocytes recovered from untreated polycystic ovarian patients. Fertil Steril 1994; 62: 353-362.
18. Barnes FL, Crombie A, Gardener DK, et al. Blastocyst development and birth after in vitro maturation of human primary oocytes, intracytoplasmic sperm injection, and assisted hatching. Hum Reprod 1995; 10: 3243-3247.
19. Barnes FL, Kausche A, Tiglias J, Wood C, Wilton L, Trounson A. Production of embryos from in vitro matured primary human oocytes. Fertil Steril 1996; 65: 1151-1156.
20. Suikkari AM, Tulppala M, Tuuri T, Hovatta O, Barnes F. Luteal phase start of low-dose FSH of follicles results in an efficient recovery, maturation and fertilization of immature human oocytes. Hum Reprod 2000; 15:747-751.
21. Trounson A, Anderiesz C, Jones GM, Kausche A, Lolatgis N, Wood C. Oocyte maturation. Hum Reprod 1998; 13 (Suppl 3): 52-62.
22. Cha KY, Han SY, Chung HM, et al. Pregnancies and deliveries after in vitro maturation culture followed by in vitro fertilization and embryo transfer without stimulation in women with polycystic ovary syndrome. Fertil Steril 2000; 73: 978-983.
23. Chian RC, Buckett WM, Tan SL. In vitro maturation of human oocytes. Reprod Biomed Online 2004; 8: 148-166.
24. Society for Assisted Reproductive Technology; American Society for Reproductive Medicine. Assisted reproductive technology in the United States: 2000 results generated from the American Society for Reproductive Medicine/Society for Assisted Reproductive Technology Registry. Fertil Steril. 2004; 81: 1207-1220.
25. Gunby J, Bissonnette F, Librach C, Cowan L; on behalf of the IVF Directors Group of the Canadian Fertility and Andrology Society. Assisted reproductive technologies in Canada: 2005 results from the Canadian Assisted Reproductive Technologies Register. Fertil Steril 2008; Epub ahead of print.
26. Chian RC, Lim JH, Tan SL. State of the art in in vitro oocyte maturation. Curr Opin Obstet Gynecol 2004; 16: 211-219.
27. Child TJ, Phillips SJ, Abdul-Jalil AK, Guleckli B, Tan SL. A comparison of in vitro maturation and in vitro fertilization in women with polycystic ovaries. Obstet Gynecol 2002; 100: 665-670.
28. Buckett WM, Chian RC, Dean NL, Sylvestre C, Holzer HE, Tan SL. Pregnancy loss in pregnancies conceived after IVM, IVF and ICSI. Fertil Steril 2008: 90: 456-450.
29. Söderström-Anttila V, Salokorpi T, Pihlaja M, Serenius-Sirve S, Suikkari AM. Obstetric and perinatal outcome and preliminary results of development of children born after in vitro maturation of oocytes. Hum Reprod 2006: 21: 1508-1513.
30. Buckett WM, Chian RC, Holzer H, Dean N, Usher R, Tan SL. Obstetric outcomes and congenital abnormalities after in vitro maturation, in vitro fertilization, and intracytoplasmic sperm injection. Obstet Gynecol. 2007; 110: 885-91.

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A follow-up on **IVF CHILDREN**

I have been very fortunate to work with Dr. Nygren on the international ACT initiative, which aims to provide people with information and guidance about the simple and effective approaches, including treatments, that can be taken to help them achieve a pregnancy. Dr. Nygren is deeply committed to his work and is world renowned for his international Assisted Reproduction Technology work, particularly with children and relating to data collection and assessment.

Naturally, I am very interested to hear about the IVF children and their well-being. We can now present a summary of Dr. Nygren's report on 16,280 of these children. Dr. Nygren's formal qualifications are as follows: Karl Nygren, MD, PhD is a clinician in the OBGYN Department of the Infertility IVF clinic at Sophiahemmet Hospital in Stockholm, Sweden. He started the first private IVF clinic in the Nordic countries, in Stockholm in 1984. He is senior adviser to the Swedish Board of Health & Welfare, Chairman of the EIMs Consortium in ESHRE, Honorary member of ESHRE and Chairman of the International Committee on the Monitory of ART. He is a member of the Assisted Conception Taskforce (ACT).

Beverly Hanck
Executive Director

A health report on 16,280 children born between 1982 and 2001, and their mothers

by KARL NYGREN, MD, PhD

BACKGROUND

In Sweden, unique circumstances make it possible to conduct retrospective register studies to follow up on the health of its citizens.

For many years, population-based health registers have collected different kinds of health data on their Swedish citizens. These registers are managed and controlled by the Swedish Board of Health and Welfare and its Centre for Epidemiology.

A unique and personal identification number, or PIN code, is assigned to each and every person in the country. Through cross-referencing, it is possible to collect data on certain individuals or subgroups of individuals whose names appear in several of these registers. The PIN codes are used extensively in community services and in all areas of health care.

STUDY DESIGN

The study ran from the birth of the first IVF child, born in 1982, until the end of 2001. The PIN codes from all 16,280 IVF children were cross-linked to five different health registers. These were The Cancer Register, The Malformation Register, The Birth Register, The Causes of Death Register and The Hospital Discharge Register.

Data from all 16,280 children born in 13,261 deliveries and their 12,186 mothers was compared to all other 2,039,943 children born in the country during these years, and their mothers. This is the largest database of its kind in the world and results from this study have recently been published in international scientific journals [1]. I am pleased to provide a summary of the results below.

TIME TRENDS

During the 20 years since the first IVF child was born in Sweden, clinical policy changed to reflect increasing understanding of the health risks associated with multiple births. Not only in Sweden, but around the world, there has been an effort to begin to reduce the number of embryos transferred. This transition has been slow in most countries so far, but more evident in the Nordic countries. In Sweden, multiple pregnancies and deliveries declined markedly during this time period. Twins decreased from 29% during 1994 to 18.5% of all IVF deliveries in 2001, and this trend has continued until today: in 2008, the proportion of IVF twins is now as low as 5% (compared to 2% in the general population)!

Triplet births also decreased from 3% to 0.5%. As a consequence, preterm births (which are strongly associated with multiple gestations) decreased from 25% to 10% (compared to 5% in the general population). Both neonatal morbidity and neonatal mortality decreased by approximately 50%.

CONGENITAL MALFORMATIONS

Major congenital malformations were reported in 5% of IVF and ICSI singletons, compared to 3% in children in the general population. A few specific diagnoses were found to have increased for singletons only, and not when comparing IVF-twins to other twins. This unexpected finding seems, to a certain extent, to be due to the fact that IVF twins are almost always dizygotic (fraternal) whereas other twins are monozygotic (identical). The malformation risk is lower for dizygotic twins.

In singletons, neural tube defects such as spina bifida, (0.3% in ICSI/IVF children compared to 0.03% in the general population) and atresias—missing or blocked passages of the gastrointestinal tract—(0.34% vs 0.18%) were seen more frequently. There was also an increased incidence of hypospadias (wrongly positioned opening on the penis, 0.46% vs 0.28%) but this was only observed after ICSI, not after IVF.

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INFANT MORTALITY

The infant mortality rate for IFV/ICSI babies was found to be 1.2% versus 0.8% in the general population, with no difference when comparing standard IVF to ICSI. There was a small but significant increase of cerebral haemorrhage (times 2), convulsions (times 1.4), respiratory problems (times 2.5) and neonatal sepsis (times 1.5) after IVF/ICSI.

CANCER RISK AND CHILDHOOD ILLNESS

There was no increased risk of cancer among IVF/ICSI children. However, hospitalisations were found to be twice as frequent until 6 years of age for IVF/ICSI children compared to naturally conceived children. This was partly explained by the increase in preterm and multiple births and might also reflect different parental attitudes seen in IVF/ICSI parents towards medical care for their children.

MATERNAL CHARACTERISTICS

IVF mothers were on average 3 years older, smoked less, more often had low or high body mass index (BMI), had more previous miscarriages, and used medications not used by mothers of naturally conceived children.

OBSTETRICAL RISKS

IVF mothers had a higher risk during pregnancy of ovarian torsion (times 10), early pregnancy bleeding (times 5), pre-eclampsia (times 1.6), blood loss at delivery (1.5), premature rupture of membranes (2.5) and caesarean section (1.4). We found no evidence that these increased medical risks were due to IVF or ICSI treatments. However, two main factors were identified as possible causes: the increased incidence of premature births (caused primarily by the increase in multiple gestations) and maternal factors, such as age and infertility problems that were not resolved by the IVF treatment.

There was a decrease in the risk of cancer in general, but reports suggested an increase in the risk of ovarian cancer in women who have had IVF/ICSI. However, it is important to understand that this risk was already present before undergoing IVF treatment, and was not increased after treatment.

There was no increase in maternal mortality between IVF/ICSI mothers compared to the general obstetric population.

SUMMARY OF OBSERVATIONS FROM THE 20-YEAR STUDY

IVF mothers differed markedly from other mothers, both pre-treatment and during pregnancy.

IVF/ICSI children had an increased risk of prematurity followed by increased risks for morbidity and mortality.

Infant malformations were somewhat increased compared to the general population.

There was no increase in the incidence of cancer among IVF/ICSI children.

Limiting the number of embryos transferred was effective. We observed a trend toward a declining proportion of multiple pregnancies and a resulting decline in health risks for both mother and child.

The vast majority of IVF/ICSI children were healthy and thriving.

CONCLUSION

We found no evidence that the increased medical risks were due to the IVF treatment itself, but rather related to multiple births and to maternal factors like age and infertility.

The medical risks related to multiple births have become more clearly understood over the last 20-25 years and IVF technology has advanced considerably. As a result, IVF clinics have begun transferring fewer embryos and achieving higher singleton pregnancy rates. Our unique opportunity in Sweden to follow the health status of both mothers and children in IVF/ICSI programs over a 20-year time period has provided further strong evidence for a shift in clinical policies worldwide towards single embryo transfer as the norm in IVF treatments.

References

Källén, B., Finnström, O., Nygren, K. and Olausson, P. (2005). *In vitro fertilization (IVF) in Sweden: Risk for congenital malformations after different IVF methods.* Birth Defects Research Part A: Clinical and Molecular Teratology 73 (3), 162-169.

Källén, B., Finnström, O., Nygren, K.G., Otterblad Olausson, P. (2005). Temporal trends in multiple births after in vitro fertilisation in Sweden, *1982-2001: a register study.* BMJ 331, 382-3.

Källén B, Finnström O, Nygren KG, Otterblad Olausson P. (2005). *In vitro fertilization (IVF) in Sweden: infant outcome after different IVF fertilization methods.* Fertil Steril, 84 (3), 611-17.

Källén B, Finnström O, Nygren KG, Otterblad Olausson P. (2005). *In vitro fertilization in Sweden: child morbidity including cancer risk.* Fertil Steril, 84 (3), 605-10.

Källén B, Finnström O, Nygren KG, Otterblad Olausson P. (2005). *In vitro fertilization in Sweden: maternal characteristics.* Acta Obst Gynecol Scand, 84, 1185-91.

Källén B, Finnström O, Nygren KG, Otterblad Olausson P., Wennerholm. U.-B. (2005). *In vitro fertilisation in Sweden: obstetric characteristics, maternal morbidity, and mortality.* BJOG, 112, 1529-35.

SUIVI DES **ENFANTS NÉS** DE LA **FIV**

J'ai eu le privilège de collaborer avec le Dr Nygren lors de la démarche du Groupe de travail en conception assistée (ACT), initiative qui a comme but de diffuser de l'information et des conseils par rapport aux moyens simples et efficaces, y compris les traitements, à la disposition de celles qui cherchent à devenir enceintes. Le Dr Nygren est totalement dévoué à sa tâche et est reconnu dans le monde entier pour son travail dans le domaine des technologies de reproduction assistée (TRA), principalement en ce qui a trait aux enfants, à la collecte et à l'étude de données.

Je m'intéresse depuis très longtemps aux enfants nés de la FIV et à leur bien-être. Nous avons enfin l'occasion de lire un résumé du rapport du Dr Nygren sur 16 280 de ces enfants. Voici une courte biographie du Dr Nygren : Karl Nygren, MD, PhD, est médecin clinicien au département d'obstétrique et de gynécologie de la clinique d'infertilité FIV à l'Hôpital Sophiahemmet de Stockholm, en Suède. En 1984, il a mis sur pied la première clinique privée de FIV des pays nordiques, à Stockholm. Il est conseiller principal du Conseil suédois de la santé et du bien-être, président du consortium des programmes européens de suivi de la FIV (EIM) de l'ESHRE (Société européenne pour la reproduction humaine et l'embryologie), membre honoraire de l'ESHRE et président du Comité international de surveillance des TRA. Il est aussi membre Groupe de travail en conception assistée (ACT).

Beverly Hanck
Directrice générale

Rapport médical portant sur 16 280 enfants nés entre 1982 et 2001 et sur leur mère

par KARL NYGREN, MD, PhD

Contexte

En Suède, des circonstances uniques permettent les études de registres rétrospectifs afin d'assurer le suivi de la santé des citoyens.

Depuis de nombreuses années, les registres de santé fondés sur la population recueillent divers types de données sur la santé des citoyens suédois. Ces registres sont gérés et contrôlés par le Conseil suédois de la santé et du bien-être et son Centre d'épidémiologie.

Un numéro d'identification personnel (NIP) unique est assigné à chaque citoyen du pays. Par liaison croisée, il est ensuite possible de recueillir des données touchant certaines personnes ou sous-groupes de personnes dont le nom figure dans plusieurs de ces registres. Les NIP sont largement utilisés dans la communauté et dans tous les domaines des soins de santé.

Concept de l'étude

L'étude couvre la période de 1982, année de la naissance du premier enfant issu de la FIV, à la fin de 2001. Une liaison croisée a été établie entre les NIP des 16 280 enfants nés de la FIV et cinq registres de santé, notamment le registre du cancer et ceux des malformations, des naissances, des causes de décès et des congés des hôpitaux.

Des données concernant 16 280 enfants nés de 13 261 accouchements, ainsi que leur mère (12 186 femmes), ont été comparées à celles des 2 039 943 enfants nés au pays pendant la même période et à celles de leur mère. Il s'agit de la principale base de données de cet ordre au monde, et des résultats de cette étude sont parus récemment dans des journaux scientifiques internationaux.[1] J'ai le plaisir de résumer ces résultats ci-dessous.

Évolution chronologique

Au cours des 20 années écoulées depuis la naissance du premier enfant conçu par FIV en Suède, les politiques cliniques ont évolué grâce à une meilleure compréhension des risques pour la santé associés aux naissances multiples. Non seulement en Suède,

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mais partout dans le monde, il y a eu un effort concerté de réduire le nombre d'embryons transférés.

Jusqu'à maintenant, cette transition s'est faite lentement dans la majorité des pays, mais elle a été plus rapide dans les pays nordiques. En Suède, les naissances multiples ont connu une baisse marquée au cours de cette période. Les naissances de jumeaux ont diminué, passant de 29 % en 1994 à 18,5 % de tous les accouchements de FIV en 2001, et cette tendance à la baisse se maintient depuis. En 2006, la proportion de jumeaux nés de la FIV s'établissait à 5 % seulement (comparativement à 2 % chez la population en général) !

Les naissances de triplés ont également connu une baisse, passant de 3 % à 0,5 %. Par conséquent, les naissances prématurées (qui sont largement associées aux grossesses multiples) ont diminué de 25 % à 10 % (comparativement à 5 % chez la population en général). Autant la morbidité que la mortalité néonatales ont chuté d'environ 50 %.

Malformations congénitales

Des malformations congénitales majeures ont été signalées pour 5 % des naissances simples issues de la FIV et de l'ICSI (l'injection intracytoplasmique d'un spermatozoïde) comparativement à 3 % pour les naissances dans la population en général. Quelques diagnostics précis ont été plus élevés pour les naissances simples, mais pas pour ce qui est de la comparaison avec les naissances de jumeaux issus de la FIV et les autres jumeaux. Ces résultats inattendus semblent être attribuables, dans une certaine mesure, au fait que les jumeaux FIV sont presque toujours dizygotes (faux jumeaux), alors que les autres jumeaux sont monozygotes (identiques). Le risque de malformation est inférieur chez les jumeaux dizygotes.

Parmi les naissances simples, les anomalies du tube neural comme le spina bifida (0,3 % chez les enfants nés de l'ICSI/FIV comparativement à 0,03 % chez la population en général) et les atrésies (passages manquants ou bloqués) du tube digestif (0,34 % comparativement à 0,18 %) ont été constatées plus fréquemment. On a aussi noté une plus grande incidence d'hypospadias (anomalie de la position du méat urinaire, 0,46 % comparativement à 0,28 %), mais seulement dans les cas d'ICSI et non de FIV.

Mortalité infantile

Le taux de mortalité infantile pour les bébés nés de la FIV/ICSI a été estimé à 1,2 % comparativement à 0,8 % chez la population en général, aucune différence n'ayant été décelée dans la comparaison de la FIV standard avec l'ICSI. Il y a eu une augmentation légère, mais significative, des hémorragies cérébrales (2 fois plus), des convulsions (x 1,4), des problèmes respiratoires (x 2,5) et de la septicémie néonatale (x 1,5) après la FIV/ICSI.

Risques de cancer et de maladie infantile

Il n'y a pas eu d'augmentation des risques de cancer chez les enfants nés de la FIV/ICSI. Cependant, les hospitalisations ont été deux fois plus fréquentes jusqu'à l'âge de six ans pour les enfants nés de la FIV/ICSI comparativement aux enfants conçus de façon naturelle. Cette constatation s'explique en partie par l'augmentation des naissances prématurées et multiples, et pourrait aussi découler de l'attitude parentale différente chez les parents d'enfants nés de la FIV/ICSI en ce qui a trait aux soins médicaux prodigués à leurs enfants.

Caractéristiques maternelles

Les mères d'enfants nés de la FIV ont en général trois ans de plus que la moyenne, fument moins, ont souvent un indice de masse corporelle faible ou élevé, avaient déjà subi davantage de fausses couches et utilisaient des médicaments que les mères d'enfants conçus naturellement ne prenaient pas.

Risques obstétricaux

Les mères d'enfants nés de la FIV avaient un risque accru pendant la grossesse de torsion ovarienne (x 10), de saignements précoces pendant la grossesse (x 5), de prééclampsie (x 1.6), d'hémorragie à l'accouchement (x 1,5), de rupture prématurée des membranes (x 2,5) et de césarienne (x 1,4). Nous n'avons décelé aucune preuve que ces risques médicaux accrus étaient attribuables aux traitements de FIV ou d'ICSI. Cependant, deux principaux facteurs ont été identifiés en tant que causes possibles : l'incidence accrue de naissances prématurées (dues principalement aux grossesses multiples) et les facteurs maternels, comme l'âge et les problèmes d'infertilité qui n'ont pas été résolus par le traitement de FIV.

Il y a eu une réduction du risque de cancer en général, mais plusieurs rapports ont suggéré une augmentation du risque de cancer ovarien chez les femmes qui avaient subi des traitements de FIV/ICSI.

Cependant, il importe de comprendre que ce risque était déjà présent avant le début du traitement de FIV et n'a pas augmenté après celui-ci.

Il n'y a pas eu d'augmentation de la mortalité maternelle chez les mères ayant eu recours à la FIV/ICSI comparativement à la population obstétrique en général.

Résumé des observations de l'étude sur 20 ans

Les mères ayant recouru à la FIV présentaient des différences marquées comparativement aux autres mères, autant avant le traitement que pendant la grossesse.

Les enfants nés de la FIV/ICSI présentaient un risque accru de prématurité, puis de morbidité et de mortalité.

Les malformations infantiles étaient passablement plus élevées comparativement à la population en général.

Il n'y a pas eu d'augmentation de l'incidence du cancer chez les enfants nés de la FIV/ICSI.

La restriction du nombre d'embryons transférés a été efficace. Nous avons observé un déclin du taux de grossesses multiples et une baisse consécutive des risques pour la santé de la mère aussi bien que de l'enfant.

La vaste majorité des enfants nés de la FIV/ICSI étaient en bonne santé et se développaient normalement.

Conclusion

Nous n'avons trouvé aucune preuve que l'augmentation des risques médicaux était attribuable au traitement de FIV en soi; elle serait plutôt liée aux naissances multiples et à des facteurs maternels comme l'âge et l'infertilité.

Au cours des 20 à 25 dernières années, nous en sommes venus à mieux comprendre les risques médicaux liés aux naissances multiples, et la technologie de la FIV a fait des progrès considérables. Par conséquent, les cliniques de FIV ont commencé à transférer moins d'embryons et à obtenir des taux de naissances simples plus élevés. La chance unique qu'a eue la Suède de pouvoir faire le suivi de l'état de santé de mères et d'enfants participant à des programmes de FIV/ICSI, sur une période de 20 ans, a fourni un élément convaincant pour l'évolution des politiques cliniques internationales vers le transfert d'un embryon unique en tant que norme dans les traitements de FIV.

Références

Källén, B., Finnström, O., Nygren, K. and Olausson, P. (2005). *In vitro fertilization (IVF) in Sweden: Risk for congenital malformations after different IVF methods.* Birth Defects Research Part A: Clinical and Molecular Teratology 73 (3), 162-169.

Källén, B., Finnström, O., Nygren, K.G., Otterblad Olausson, P. (2005). *Temporal trends in multiple births after in vitro fertilisation in Sweden, 1982-2001: a register study.* BMJ 331, 382-3.

Källén B, Finnström O, Nygren KG, Otterblad Olausson P. (2005). *In vitro fertilization (IVF) in Sweden: infant outcome after different IVF fertilization methods.* Fertil Steril, 84 (3), 611-17.

Källén B, Finnström O, Nygren KG, Otterblad Olausson P. (2005). *In vitro fertilization in Sweden: child morbidity including cancer risk.* Fertil Steril, 84 (3), 605-10.

Källén B, Finnström O, Nygren KG, Otterblad Olausson P. (2005). *In vitro fertilization in Sweden: maternal characteristics.* Acta Obst Gynecol Scand, 84, 1185-91.

Källén B, Finnström O, Nygren KG, Otterblad Olausson P., Wennerholm. U.-B. (2005). *In vitro fertilisation in Sweden: obstetric characteristics, maternal morbidity, and mortality.* BJOG, 112, 1529-35.

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DONATION AND DISCLOSURE

A recent German study finds donors open to change

by PETRA THORN *Adapted for Creating Families by* ***Naomi Louder.***

The availability of donor semen is a hot button issue in the world of assisted reproduction. Donor semen is needed by couples experiencing male factor infertility or at severe genetic risk for disease, by lesbian couples and by single women, and the regulations regarding the collection and distribution of donor sperm have recently been changed or are under review in many countries worldwide, including Canada.[1] Among the questions that have been raised are the issues of donor compensation—whether donors should be paid for their contribution, and how much; and anonymity—should donation remain private and secret, or do the children resulting from the use of donor sperm have the right to know their genetic history? A recent German study looked at several aspects of the donor profile, focusing on the motivation and attitude of donors, and their position on the issue of disclosure.

In Germany, DI was traditionally performed behind closed doors, with the anonymity of donors guaranteed to the point of destroying records after a requisite 10-year period. In 2006, a drastic change: with the release of the European Tissue Directive, clinics are now under obligation to maintain records. These changes in the regulation of DI have only entered German legislation with respect to the documentation of donated organs and tissue; in a revision of German Organ Transplantation Act, records must now be maintained for a minimum of 30 years, but there is no provision for offspring to be granted access to these records. In German case law, it has been proven that offspring have the right to identify a biological parent, but no case involving parental disclosure after DI has ever been tried in German courts.

According to the professional guidelines of the German Medical Chamber (GMC), donors must agree for their identity to be disclosed to offspring and would-be parents must agree for the disclosure to occur. The GMC guidelines have other recommendations as well: for example, lesbian couples and single women are excluded from access to DI on the basis that two parents, one male and one female, are necessary to raise a child. Naturally this stipulation has caused concern among the groups touched by it, and it is unclear whether the GMC in fact has the legal right to circulate such a discriminatory policy. The GMC guidelines are *not* informed by another salient question: under German law, female couples and single women have the right to access DI, but in a case where there is no male parent, the donor could be held legally responsible for the child that bears his genes.

Clearly, the issues at stake in the legislation of DI in Germany are far from simple, and regulatory changes have not yet succeeded in disentangling the threads of debate. In the last 15 years, the issue of donor insemination and other fertility issues have come more into the public eye. In 1995, Dr. Petra Thorn organized the first public preparation seminar for DI, open to all those who were interested. More than twenty subsequent seminars have proved the need and popularity of such a forum, with attendees reporting higher levels of confidence and comfort with the prospect of DI, and with the vast majority expressing a clear intention to disclose their use of DI to the potential children.[2] Through these seminars and other initiatives, as well as the growing visibility of fertility issues in the German media, the voices of single women and lesbian couples questioning the restrictions placed upon them, and the efforts of adult children of DI speaking out for disclosure, the climate in Germany has become much more open.

In a national 2006 study, Dr. Thorn, together with colleagues, explored the attitudes and motivation of donors: their demographic groups, their reasons for donating, their interest in the outcome and knowledge of current legislation, willingness to donate to specific groups, their attitude towards payment and towards disclosure. Of the 15 clinics in Germany that recruit donors, 13 participated in the study, sharing the number of current donors and circulating a questionnaire to the latter.[3]

The results show that the average donor is likely to be a young, educated man (88%), without prejudice in the matter of who receives his sperm (68% willing to donate to lesbian couple, 56% to a single woman). He may be married or in a serious relationship (54%), or single (41%), and there is a good chance he has had personal contact with someone experiencing infertility (48%). He might have a child of his own (25%), but likely does not (75%); he might be looking for financial gain (42%), or again he might be hoping to help an infertile couple (42%), but he almost certainly believes he should be compensated financially for his donation (98%).

In the matter of disclosure, it is difficult to pinpoint even approximately the average donor's attitude—the largest group, by a narrow margin, were in favour of disclosure (37%), but a similar number were unsure (34%) or against (29%). However, 43% of donors were willing to be contacted by adult children born through their donations. Some of the men made additional comments. Those in favour of disclosure cited that it would "prevent later problems," that it was key to the formation of an identity, or simply that "it is everyone's right." Those who were against feared that knowledge of origins "could confuse the child," or that it "could lead to problems."

A recent German study looked at several aspects of the donor profile, focusing on the motivation and attitude of donors, and their position on the issue of disclosure.

Most of the men surveyed relied on the clinic for legal information, although some reported doing additional research, but 60% assumed that they had no legal responsibility towards offspring. This might be assumed to have an impact on their attitude towards disclosure, and towards donation to family configurations without a social father, where the prospect of legal responsibility for a child might trump ethical concerns.

The results of this study are of the essence at a time when the regulations governing donor insemination are key to determining the accessibility of donor sperm. In Canada, the Assisted Human Reproduction Act disallows payment of donors, and as a result the reserves of donor sperm are being depleted, with few donors available to replenish them. Research that sheds light on the mentality of donors could be invaluable to the recruitment of new donors. It is encouraging to see that in Germany, attitudes towards DI are changing, giving way to a new openness towards the idea of disclosure and of a less restrictive and secretive version of DI. It is to be hoped that greater openness and understanding of this issue, in Germany, in Canada and worldwide, can lead to the development of a truly equitable system of regulation that will answer the current needs of donors and would-be parents, and the future needs of the children DI can produce.

References

1. Del Valle AP, Bradley L, Said TM. Anonymous semen donor recruitment without reimbursement in Canada. *Reproductive BioMedecine Online.* 2008; 17, Suppl. 1: 15–20.

2. Thorn P, Daniels K. A group work approach in family building by donor insemination—empowering the marginalized. *Hum Fertil.*2003;6:46–50.

3. Thorn P, Katzorke T, Daniels K. Semen donors in Germany: A study exploring motivations and attitudes. *Hum Reprod* 2008 23(11):2415–2420.

YOUR FIRST APPOINTMENT
WHAT TO EXPECT

by ELLEN M. GREENBLATT, MD, FRCSC

One in six couples experience infertility, and it is estimated that 250,000 Canadians who are having difficulty conceiving are not seeking treatment. For many couples, it is difficult to accept that there may be a problem. Couples often delay seeking treatment because of denial, nervousness about disclosing information concerning a very intimate part of their lives, shame, guilt and fear of what the assessment will involve, and what may be discovered. These worries are justifiable and very natural, but like many other medical diagnoses, the earlier infertility is discovered, the better your chances of successful treatment.

This article will let you know what to expect from your initial consultation with a specialist in fertility problems. The first appointment may be the hardest in terms of making the decision to seek help and then go through with it, but let's take the mystery out of the appointment itself.

The initial consultation and generally all visits to your specialist should be attended by both partners, unless the person seeking treatment is single. You can expect the initial visit to require an hour to an hour and a half of your time.

Some clinics will have already had you fill out a questionnaire. The American Association of Reproductive Medicine (ASRM) questionnaire is a common starting point, and this form or something similar may have been sent to you already. It can be a starting point to document relevant prior medical and reproductive history.

History

At your first visit, your physician will ask you questions with the aim of ascertaining your detailed medical history.

Female history. This will focus on reproductive and menstrual history, and include information about any previous pregnancies as well as details of your menstrual cycles, and accompanying symptoms, such as pelvic pain. A detailed contraceptive history will be recorded. Symptoms that can be a hallmark of ovulation disorders, such as acne and excess hair growth, will be sought.

A detailed reproductive and gynecologic history will include recording how regularly you've had PAP tests, any exposure to sexually transmitted infections, and any episodes of pelvic

infection. Details of any previous infertility tests or investigations and previous infertility treatments will be important.

A history regarding your general health, previous or ongoing illnesses and surgical history, especially operations within the abdomen and pelvis, medications you are on and any allergies will be recorded. Family history will be reviewed, especially illnesses that can be hereditary, in order to help plan for a healthy pregnancy.

Information about your work and working hours and environment, the use of tobacco, alcohol and substances is important. Changes in body weight and exercise patterns are important details as well.

Male history. The general medical, surgical and family history, as detailed above, will be reviewed. Emphasis will be on previous genital or prostate infections, trauma or surgery to, or near, the reproductive organs. Occupation and exposure to environmental factors (heat, vibration, chemicals, pesticides) will be elicited. General health, weight and exercise patterns are important, as well as exposure to prescribed medications, tobacco, alcohol and other non-prescribed substances.

Couples history. Frequency and timing of sexual intercourse will be reviewed, as well as any difficulties experienced such as pain during intercourse, difficulties with erection or ejaculation. The number of lifetime sexual partners and a history of pregnancy during a prior relationship are all important details that will guide future investigations.

Examination

Female. A general examination will include height, weight, and blood pressure. A focused physical examination of the abdomen, and a gynecologic and internal bimanual pelvic examination will be performed. The pelvic examination is aimed at identifying any masses that can be signs of uterine enlargement due to fibroids or ovarian cysts, and to check for tenderness or nodules that can be associated with endometriosis, or signs of immobility associated with scarring due to infection, endometriosis or previous surgery. Many specialists will perform a transvaginal ultrasound at the same examination, which will assist in the evaluation of these conditions as well. A PAP test and evaluation for any infections of the vagina and cervix may be done at this time.

Male. Depending on the practice of the clinician, an examination of the male genitalia may or may not be performed. Some clinicians will defer this until after semen analysis has been performed.

Investigation

Basic investigations will focus on the evaluation of the three essential factors required for pregnancy to occur: ovulation (monthly egg release), the functioning of ovaries and fallopian tubes, and the quality of semen.
Ovulation. Determination of normal ovulation (monthly release of an "egg") often can be determined by reviewing menstrual history. A history of regular menstrual cycles, usually indicated by a cycle length of 25-35 days, the presence of pre-menstrual symptoms such as breast tenderness and bloating, and

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cramping with periods, is taken to indicate that ovulation has occurred normally. If it is unclear by history alone as to whether ovulation is happening, other methods to evaluate the menstrual cycle may include "cycle monitoring" (periodic blood tests and ultrasound assessment) during one menstrual cycle, or measurement of blood progesterone levels performed half way between the predicted day of ovulation and the anticipated next start of the menstrual cycle (for example a day-21 blood test for a typical 28 day cycle) in order to document ovulation.

Assessment of Fallopian Tubes and Uterine Cavity. For normal conception to occur, sperm and egg must be able to meet, and this happens in the fallopian tubes. The best way to evaluate the anatomical relationship of the fallopian tubes and ovaries is a laparoscopy. However, this is an operation performed under general anesthetic, and is not usually the first method of evaluation in most women. Laparoscopy is usually only considered as the first step if there is a significant reason to suspect disruption in the function of these organs (such as a history of pelvic infection or sexually transmitted disease, or signs, symptoms or clinical findings suggestive of endometriosis). In many women, the condition of the fallopian tubes and contour of the uterine cavity can be initially assessed by less invasive tests, such as a hysterosalpingogram (HSG) or sonohysterogram. An HSG is a test in which a contrast liquid (a dye) is slowly injected into the uterus through a small catheter placed through the cervix. X-rays are taken during the injection of the dye, and images are recorded to show the uterine cavity and the fallopian tubes as the dye runs through the fallopian tubes, demonstrating that there is no blockage. A sonohysterogram is similar. In this test sterile water or saline solution is flushed into the uterine cavity through a catheter, and a transvaginal ultrasound is performed simultaneously. Ultrasound pictures are taken demonstrating the uterine contour. Although the fallopian tubes cannot be followed throughout their length by this technique, a fallopian tube is likely unobstructed if air bubbles are seen flowing through the initial segment of the fallopian tubes, where they leave the uterus, if fluid does not appear to collect within the tube, and a collection of free fluid is subsequently demonstrated in the pelvis.

Male Factor. The male factor is evaluated by examining an ejaculated sperm sample. Ideally, a sperm sample should be collected at the lab where it will be examined. The period of abstinence from ejaculation (by intercourse or masturbation) should have been no less than two days and no longer than five days. The sample is collected in a sterile container by masturbation. If a sperm sample cannot be produced at the lab, then it should arrive at the lab within one hour of production and be kept at body temperature (for example, by placing in the underarm) while transporting it. One of the most important factors in evaluating the results of a semen sample is the quality and experience of the lab performing the test. As a semen analysis evaluates several quantitative and qualitative factors of a semen sample, an experienced andrology lab that routinely evaluates a high volume of semen samples each year is needed. A semen analysis performed at a center that rarely evaluates these samples can be misleading. As semen samples normally fluctuate over time, and because the life cycle of sperm production is almost three months, more than one sample over several months may be required to get a true picture of sperm quality. Any abnormalities would be followed up by an adequate urologic evaluation, which will include a physical examination, blood tests and possibly an ultrasound evaluation.

Other Tests. Other routine blood tests that may be ordered would include blood type and presence of any blood

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Other tests that may be ordered to assess ovarian function would include menstrual cycle day three hormone evaluations and transvaginal ultrasound, and if there is any concern regarding the regularity of ovulation, evaluation of thyroid function and prolactin levels. If it is very likely that the couple will progress with some form of assisted reproductive treatment, blood tests that are required prior to almost any fertility treatments include evaluation of the presence of communicable viruses (hepatitis B, hepatitis C, syphilis exposure, HIV virus). Often all blood tests are ordered at once in order to minimize the time required to make a diagnosis and maximize the ability to offer a treatment plan. Generally, all evaluations, including blood tests, tubal assessment, viral screening, ultrasounds, and semen analysis can occur over one to two months.

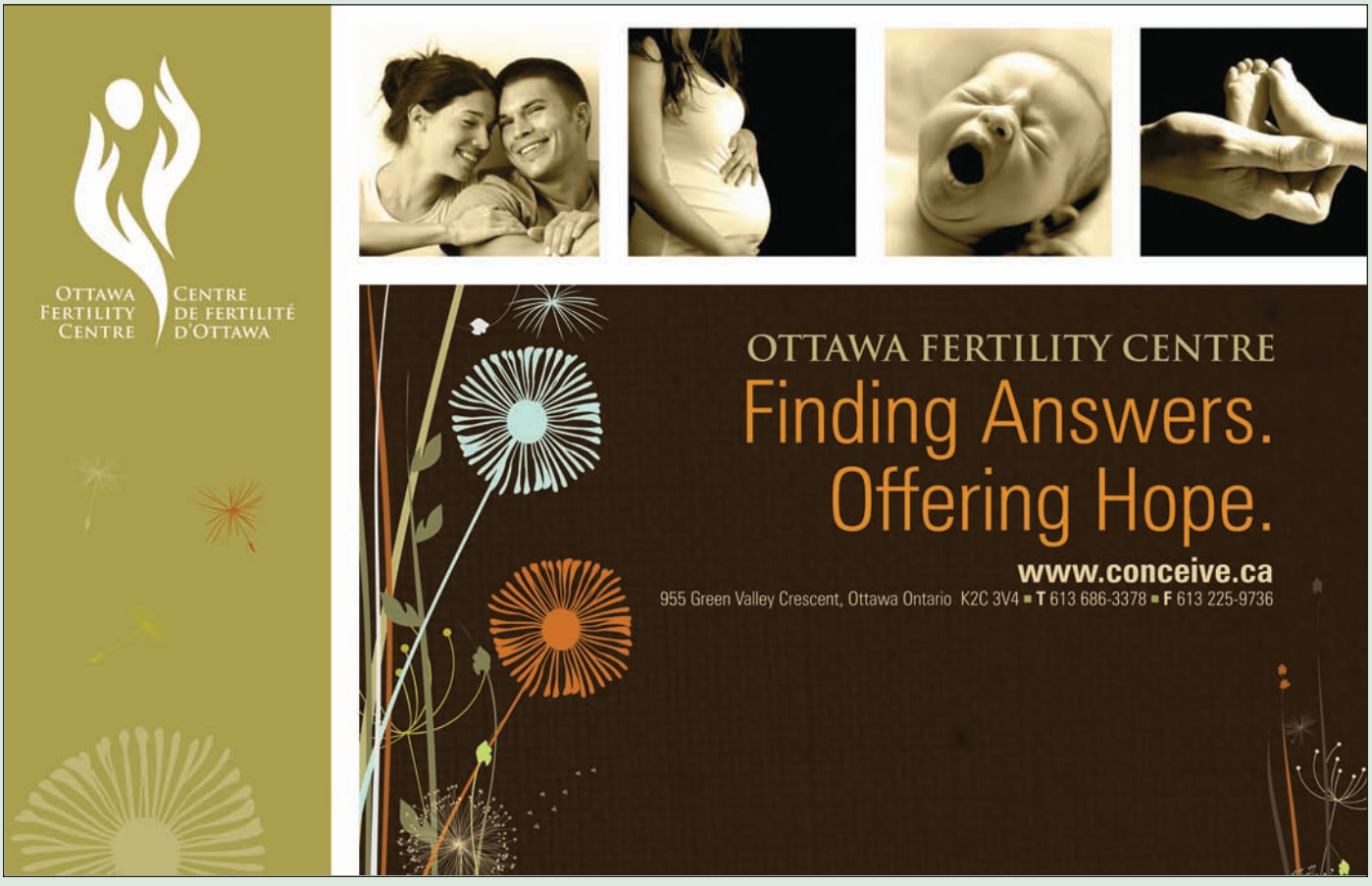
In approximately 85% of cases, a diagnosis will be made towards which a treatment plan can be tailored. A female cause of infertility is found as often as a male cause (approximately 30% each). In a third of couples, both female and male factors may be present that are interfering with natural conception. In approximately 15% of couples, no obvious abnormality is found and the label "unexplained" infertility is used, which really just means that all known causes have been ruled out. A diagnosis of unexplained infertility does not mean that nothing can be done to increase the chances of pregnancy, and fertility treatments can increase the likelihood of conception even when there is no obvious problem.

Although it may seem overwhelming to begin a fertility evaluation in the case of delayed conception, you should remember that your fertility doctor is there to help you achieve your goal of forming a family. A normal evaluation after a short duration of infertility may be all that is required to reassure you that there is no major problem and that you should keep trying. If an obvious factor is found, then a more directed solution can be planned.

It is important to remember that increasing female age has a marked negative effect on the ability to conceive naturally, as well as on the likelihood of success with all forms of fertility treatment. Delaying a fertility evaluation for several years while waiting for "nature to take its course" may therefore not be in your best interests. Be proactive with your own health and reproductive life plans and you are less likely to regret what might have been.

About the author

Ellen M. Greenblatt, MD, FRCSC, is the clinical director of reproductive biology and IVF units, Division of Reproductive Sciences, and the RE&I Fellowship Programme Director at Mount Sinai Hospital's Department of Obstetrics and Gynecology in Toronto. She is also an Associate Professor of the University of Toronto.



Assisted reproduction in Belgium

The success of eSET and beyond

by ILSE DELBAERE, PETRA DE SUTTER, JAN GERRIS AND MARLEEN TEMMERMAN

Belgian researchers have played a pioneering role in assisted reproductive technology (ART) and their expertise extends from technical procedures to recommendations on how to improve the quality of in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) treatments. One major adverse effect of assisted reproduction is multiple pregnancy, to the point where the rate of multiple birth associated with ART was sometimes called the "twin epidemic." Twin and multiple births may be dangerous for mothers and infants, and are tremendously costly to the health care system. Today, the Belgian government is one of the few worldwide to implement satisfactory medical coverage for assisted reproduction, offsetting the cost by implementing a simple strategy to reduce ART-related multiple births.

To address the high incidence of multiple births after IVF, early Belgian studies compared pregnancy rates after double embryo transfer (DET) to pregnancy rates after single embryo transfer (SET). They concluded that elective single embryo transfer (eSET) is the only way to significantly reduce multiple pregnancies. These studies also showed huge savings to healthcare when twin pregnancies were reduced, and the Belgian government therefore decided to fund up to six IVF/ICSI cycles per couple, providing SET was applied whenever possible. The introduction of this law in 2003 had a significant effect on the twin pregnancy rate in Belgium and further studies revealed distinct advantages for children after SET.

Assisted reproduction in Belgium: a short history

The first Belgian IVF baby was born in 1984, at which time most European countries were beginning to have success with IVF treatment. IVF was to be the long-awaited answer for women who suffered from blocked or damaged fallopian tubes.

In the early days of assisted reproduction, the techniques were less efficient than they are today. In order to achieve acceptable pregnancy rates, multiple embryos were transferred to the uterus after IVF or ICSI. This procedure increased the chance of becoming pregnant; it also increased the chance of conceiving twins or higher order multiples[1]. There is a high incidence of preterm births in twins. They are at risk for low or very low birth weight, while the risk of late miscarriage or stillbirth in twin pregnancies is high. Higher order multiple births—triplets, quadruplets, and higher—are at an even greater risk[2]. Some of other risks to mother and infant in a multiple birth situation include: obstetric complications, hypertension, pre-eclampsia, preterm labour, anaemia, increased caesarean section rate; fetal or neonatal risk for increased mortality, lower gestational age, lower birthweight, respiratory distress syndrome, cerebral palsy and long-term neurological complications[6].

To reduce higher order multiple births, Scandinavian and Belgian studies in the late nineties assessed the efficacy of DET [4], the practice of limiting the number of embryos transferred to two. DET indeed helped to lower the rate of higher order multiple pregnancies after ART without having much adverse effect on the pregnancy rates. However, the incidence of twin pregnancies after ART did not change.

The next logical step was to assess single embryo transfer. Early studies comparing the pregnancy rates after DET versus SET had been disappointing in terms of the pregnancy rates achieved[5]. However, these results were biased: the SET group included women with only one embryo available for transfer. This type of SET is called compulsory SET (cSET), in that there is no alternative but to transfer the one available embryo. Studies including women with several embryos available for transfer, on the other hand (SET or eSET), showed far better pregnancy rates. Although the pregnancy rates after eSET were somewhat lower, it was always possible to cryo-preserve one or more embryos after eSET to use for subsequent cycles. One study compared a group undergoing a cycle of DET to a group undergoing SET. In the SET group, if the first, fresh IVF cycle did not result in pregnancy, a second cycle was performed with a cryo-preserved embryo. The pregnancy rate for this group was 30.7%, where the pregnancy rate for a normally fertile couple was approximately 30%[6]. It seems that SET can provide an acceptable pregnancy rate.

Embryo selection is crucial in the eSET procedure. Some embryos have higher implantation potential than others, so it is important to select the most suitable embryo to transfer. In addition to embryo quality, young maternal age (under age 36) is another important determinant of success with eSET[7]. It was found that young women with two good quality embryos transferred in their first two attempts had the highest chance of a twin pregnancy (twin prone patients). These women are therefore ideal candidates for SET, as they are most likely to achieve pregnancy.

Health econonomic issues, government measures, and repercussions of twin pregnancies

Prior to 2003, some medical costs for ART were already reimbursed by the Belgian national health care system. Medication, physician visits and monitoring costs were covered, while laboratory costs were paid by patients. One IVF attempt cost patients about 1600 CAD and one ICSI attempt, 2000 CAD. These were significant sums for most people, and for some patients they were prohibitive. Because the Belgian social security system aims to provide equal health services for all social classes, they had discussed changing this situation for some years, but resources were limited.

Health economic studies showed how the use of SET could provide a viable solution. Multiple pregnancies, especially the large number of twin pregnancies brought about by DET[8], were found to be very costly to healthcare. Over the years, studies have shown twin and multiple pregnancies to be extremely costly on a number of levels, including deliveries and neonatal care; social costs incurred through the exaggerated stress levels experienced by parents responsible for two or more children; and the lifelong support needed for disabled children.

As pregnancies after SET result primarily in singletons, SET is substantially cheaper than DET in terms of costs to healthcare. These findings encouraged the Belgian government to introduce a reimbursement law for IVF/ICSI, and since July 2003, up to six IVF/ICSI attempts per couple are reimbursed in women aged up to 42 years. Single embryo transfer is systematically performed in first attempts of women aged 35 or younger.

Legal number of embryos to transfer

Women up to 35 years + 364 days old:

- First cycle: transfer one fresh embryo or maximum two cryopreserved embryos
- Second cycle: transfer one fresh embryo if good quality embryo available. If no good quality embryo available, two embryos may be transferred.
- Third cycle on: transfer maximum of two fresh embryos

Women aged 36 – 39 years:

- First and second cycle: transfer maximum of two fresh embryos
- From third cycle on: transfer maximum three fresh embryos

Women aged 40 – 42 years:

- No limitation to number of embryos transferred

With this protocol in place, it was estimated that the risk of triplet pregnancies could be eliminated, and that twin pregnancies could be reduced by half.

In 2004, the effect of this government measure was already visible in the birth statistics (fig.1). In Belgium, the female age distribution in infertility programs ranges from 26 to 43 years old, with a median age of 33.7 years. In 2005, 5342 transfers of a single embryo were performed out of 14,363 cycles in women aged up to 35 years (37%). In the first cycle, eSET was performed in 97% of the cases, in the second cycle 49% of patients aged 35 or younger received eSET.

The figures above represent the rate of twin pregnancy in all types of conception (naturally conceived and assisted reproduction). The overall rate of twin pregnancy has been reduced by half through the use of SET in ART.

Success in the reduction of twin pregnancies and beyond

The transfer of one embryo in IVF/ICSI procedures substantially reduced the twin pregnancies. However, singletons after ART were found to have poorer outcomes (higher incidences of preterm birth and low birth weight, for example) when compared with naturally conceived singletons, whereas studies comparing naturally conceived twins with twins after assisted reproduction hardly found any difference between both groups[9].

Recent Belgian studies therefore focused on singletons after eSET, and compared these children with naturally conceived singletons[10] or singletons after DET[11]. These studies showed that the incidences of preterm birth and low birth weight are

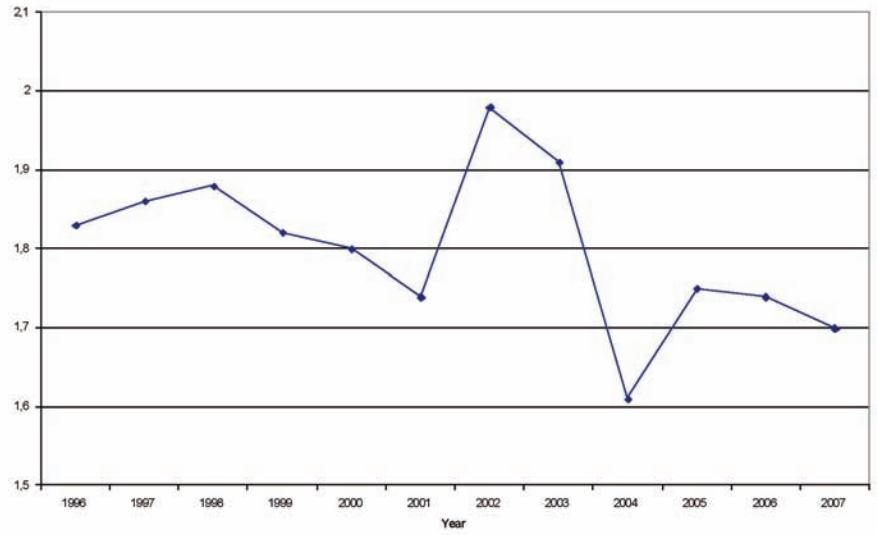


Figure 1. Evolution of twin pregnancies in Flanders, Belgium (% of total deliveries)

considerably less in singletons after eSET when compared with singletons after DET, and are even comparable with naturally conceived singletons.

It was hypothesized that singletons after SET fare better than singletons after DET due to a vanishing twin effect in the latter group. Pinborg et al. indicated a difference in birth weight of 178 grams between singletons who started as a twin and "real singletons," in favour of the latter group [12]. In the study of De Sutter et al., seven percent of the singletons after DET started as a twin (two gestational sacs were seen at first ultrasound). However, in the weeks before this first ultrasound there may have been more vanishing twins in the DET group. Moreover, another study reported a higher incidence of first trimester bleeding in singletons born after DET compared with singletons after SET, which may also indicate vanishing twin syndrome.

There is still room for improvement

Although the number of twins decreased substantially in 2004, in 2005 a new increase was observed with a status quo in 2006 and 2007 (fig. 1). Probably this trend was attributable to the notable success of the IVF reimbursement policy, which led to a substantial increase in the number of patients entering infertility programs. Furthermore, young women who had entered the program in 2003 but had not yet conceived might have evolved to a second or third cycle, in which more embryos are transferred. Since a large number of these women became pregnant with twins, we recommend further exploration of the possibilities of SET in women aged 35 to 40 with good quality embryos available, as a growing number of patients entering infertility programs are in this age group. The possibility of SET in cryo-cycles also merits further exploration.

Conclusion

The implementation of SET has proven to reduce the rate of twin pregnancy in Belgium. The government decision to pay for IVF cycles while implementing SET is wise on a number of levels: firstly, it greatly reduces the health risk posed to mothers and infants by ART-related multiple birth; secondly, it allows fairer access to IVF, serving those who need it, not merely those who can afford it; and finally, it reduces the enormous cost of complications related to multiple births. Added to this, the discovery that singletons after SET are often born healthier than singletons after DET is very encouraging, and gives more reason to continue the practice of SET and explore further possibilities. For many years, the "success" of IVF has been measured by how many pregnancies are achieved, with a reluctance to do anything that might decrease the pregnancy rate even slightly. But as technologies improve, our goal should be a healthy outcome for mother and child.

References

[1] Bergh C. Single embryo transfer: a mini-review. Hum Reprod 2005; 20(2):323-327.

[2] Gerris J, De Neubourg D, Mangelschots K, Van Royen E, Vercruyssen M, Barudy-Vasquez J et al. Elective single day 3 embryo transfer halves the twinning rate withoud decrease in the ongoing pregnancy rate of an IFV/ICSI programme. Hum Reprod 2002; 17(10):2626-2631.

[4] Staessen C, Janssenswillen C, Van Den Abbeel E, Devroey P, Van Steirteghem A. Avoidance of triplet pregnancies by elective transfer of two good quality embryos. Hum Reprod 1993; 8(10):1650-1653.

[5] Elsner CW, Tucker MJ, Sweitzer CL, Brockman WDW, Morton PC, Wright G et al. Multiple pregnancy rate and embryo number transferred during in vitro fertilization. Am J Obstet Gynecol 1997; 177(350):357.

[6] Dhont M. Single-embryo transfer. Seminars in Reproductive Medicine 2001; 19(3):251-258.

[7] Gerris JMR. Single embryo transfer and IVF/ICSI outcome: a balanced appraisal. Hum Reprod Update 2005; 11(2):105-121.

[8] Gerris J, De Sutter P, De Neubourg D, Van Royen E, Van der Elst J, Mangelschots K et al. A real-life prospective health economic study of elective single embryo transfer versus two-embryo transfer in first IVF/ICSI cycles. Hum Reprod 2004; 19(917):923.

[9] Helmerhorst FM, Perquin DAM, Donker D, Keirse MJNC. Perinatal outcome of singleton and twins after assisted conception: a systematic review of controlled studies. BMJ 2004; 328:7434.

[10] De Neubourg D. The obstetrical and neonatal outcome of babies born after single-embryo transfer in IVF/ICSI compares favourably to spontaneously conceived babies. Hum Reprod 2006; 21(4):1041-1046.

[11] De Sutter P, Delbaere I, Gerris J, Verstraelen H, Goetgeluk S, Van der Elst J et al. Birth weight of singletons after assisted reproduction is higher after single than after double embryo transfer. Hum Reprod 2006; 21(10):2633-2637.

About the Authors

The authors are researchers and clinicians from Ghent University Hospital, a major infertility centre and IVF unit in Belgium, and pioneers of single embryo transfer. They have a national and international reputation for their patient-centred high quality care and innovating research and can be reached at www.arg-uzgent.be. Petra De Sutter is holder of a fundamental clinical research mandate by the Flemish Foundation for Scientific Research (FWO-Vlaanderen). Contact: Ilse Delbaere, P3, De Pintelaan 185, 9000 Ghent. Phone: 0032 9 332 48 53, Fax: 0032 9 332 38 31, ilse.delbaere@ugent.be