

Women undergoing treatment with in-vitro fertilization (IVF) face an increased risk of twins and triplets. The social and economic consequences, as well as risks to the mother and baby (babies), are higher with multiple pregnancies as compared to singletons.

The incidence of twins and high order multiple gestations (triplets and higher) has risen dramatically over the past two decades. Twin pregnancies have risen 52%, while high order multiple pregnancies have increased 404%. This rise is mainly due to the increased use of fertility drugs for superovulation (trying to make more eggs) and for assisted reproductive technologies (ART), as well as increased utilization of IVF.

Competition between ART programs, coupled with the lack of insurance coverage for ART throughout North America, has generated intense pressure to achieve success in a minimal number of cycles.

Often, infertility couples consider the birth of twins acceptable, or even desirable, since it results in an instant family after (sometimes) years of infertility. Multiple pregnancies can result in the following maternal complications:

- ◆ Miscarriage
- ◆ Hemorrhage
- ◆ Pregnancy induced high blood pressure
- ◆ Diabetes
- ◆ Anemia
- ◆ Cesarean Section is often needed in twin pregnancy
- ◆ Prolonged hospitalization resulting in higher cost of medical care

Fetal complications associated with multiple pregnancies include:

- ◆ Preterm delivery. The average length of a single pregnancy is 39 weeks; 35 weeks for twins; and 33 weeks for triplets. The proportion of twins and triplets delivering



The
QUEST
for
Single Embryo Transfer
Dr. Ken Cadesky

before 30 weeks is 7% and 15%, respectively. These babies are more likely to develop serious, lifelong health problems, such as cerebral palsy (CP) and other neurological disabilities. The rate of CP in twins is 8 times greater and is 47 times greater in triplets

- ◆ Low birth weight. The lifelong disability rate is 25% for babies weighing less than 1 kg at birth
- ◆ Increased stillborn and neonatal death rates. Singles have a 1% chance; 4.7% for twins; and 8.3% for triplets
- ◆ Birth defects in twins are twice as common than in single births

The ideal ART outcome is the delivery of a single, healthy child. There are a number of strategies that we at LifeQuest have instituted in order to progress toward this goal. The ultimate aim is to transfer fewer embryos of higher quality to maximize pregnancy rate and minimize multiple gestations.

LifeQuest is one of only a few ART centers in Canada that does almost exclusively Day 5 (blastocyst) embryo transfers instead of Day 3. For the first 3 days of an embryo's life, the culture environment in the dish that it's living in is supporting it. At about 3 1/2 days the "genetic blueprint" (genome) of the embryo "turns on" and it becomes more and more responsible for

continued survival on its own. By waiting until Day 5, we can allow natural selection to occur by weeding out embryos with very little chance of continued survival. We can now transfer fewer embryos by waiting until Day 5. In a Day 3 transfer, we have no way of knowing which embryos will survive and which will die a natural death. As a result, more Day 3 embryos are employed per transfer and, therefore, there is a significant increase in multiples.

The only way that a high order multiple pregnancy can then be prevented is with selective reduction, a surgical procedure that destroys one or two embryos for the benefit of the others that remain. This has both emotional and potential medical implications for the couple and their remaining embryos.

At LifeQuest the current policy is to transfer no more than two Day 5 embryos in women under age 40, unless there are unusual circumstances. With this policy, we still have a twin rate of at least 1 in 4. The ideal situation would be to transfer only one healthy embryo.

Current studies estimate that over 50% of embryos are genetically abnormal (even on Day 5). This is why when two embryos are transferred; a single pregnancy most often results (about 66-75% of the time).

The most extreme method of preventing multiple pregnancies is single embryo transfer (SET). A number of studies are currently underway in order to assess the feasibility of SET. Most show a lower pregnancy and live birth as compared to double embryo transfer. In Belgium, pregnancy rates equaling double embryo transfer rates have been achieved by utilizing the combination of SET and later frozen embryo transfer. Most European countries

continued

THE QUEST FOR SINGLE EMBRYO TRANSFER, *continued*

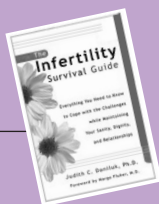
subsidize IVF: the added cost of a frozen cycle is not costly to the patient. As well, the standard in Europe is to transfer Day 3 embryos, with an average pregnancy rate lower than 35%. LifeQuest averages pregnancy rates above 45%.

Since at least 50% of embryos are genetically abnormal, would it make sense to analyze embryos before they are transferred in order to choose only genetically normal ones for transfer? This would require PGD (preimplantation genetic diagnosis), a procedure offered at LifeQuest that genetically analyzes embryos on Day 3 in order to choose normal ones for transfer on Day 5. PGD is invasive and, although complications are rare, can damage the embryo.

Utilization of SET will likely increase as methods of predicting embryo viability improve. A number of methods to determine embryo competence though noninvasive techniques are active areas of investigation at LifeQuest and around the globe.

Government legislation preventing multiple pregnancies as a result of IVF is likely to occur in the near future. We at LifeQuest are pleased that our philosophy and policies have that same goal in mind. ♦

Suggested Reading



The Infertility Survival Guide:

Everything You Need to Know to Cope with the Challenges While Maintaining Your Sanity, Dignity, and Relationships

Author: Judith C. Daniluk, New Harbinger Publications, 2001

At LifeQuest Centre for Reproductive Medicine, we engage in ongoing clinical research for the advancement of our own knowledge of infertility, and ultimately, through the development of safer and more advanced methods of treatment as well as improved clinical results, for the benefit of our patients. It is our hope that with technical and scientific advancements, the chances of conceiving may increase without compromising the safety of the patient and baby. The following are some of the areas we have chosen to pursue in clinical research:

Sperm Chromatin structure is an area of interest at LifeQuest. We have embarked on a controlled, randomized trial with the Urology department at Mount Sinai Hospital in Toronto. During this trial, we are hoping to measure and compare sperm chromatin structure of different sperm and testicular specimens so that we may predict the quality of a specimen used for intracytoplasmic sperm injection (ICSI). Measuring chromatin structure shows the susceptibility of the sperm to damage. Recent literature has shown high levels of chromatin damage in the sperm can adversely affect embryo quality and implantation success.

Freezing oocytes is an ongoing project at LifeQuest. Since the first live birth of a baby from our method in 2004, we are continuing with this study on a case-by-case basis. Our method is a modification of the 'slow freezing' method used by Italian researchers in 2002 (Fabri et al). This process will eventually allow fertility preservation, and the possibility of banking donated oocytes in the same way sperm banks are available to patients.

T.E.R.M. Program: Dr. Carl Laskin, Director and Managing Partner at LifeQuest, has had a clinical research

LifeQuest Research Update

programme in effect for more than 20 years investigating causes of recurrent miscarriage. The T.E.R.M. programme (Treatment and Evaluation of Recurrent Miscarriage)

recently completed a large randomized clinical trial (the HepASA trial) that compared two treatment protocols for women with a history of recurrent miscarriage. Women in that study had specific autoantibodies in their blood (antiphospholipid antibodies) that could interfere with fetal development either early in the pregnancy, preventing proper embryo implantation, or later on, interfering with blood supply to the growing fetus.

The T.E.R.M. Programme is currently the only Canadian centre participating in an international observational 5-year trial funded by the National Institutes of Health (NIH) in the US called the PROMISSE study. Blood and urine samples are collected throughout pregnancy from women with and without a history of pregnancy loss and autoimmune disease. The samples are monitored for the presence of autoantibodies and proteins involved in the coagulation process in an attempt to better understand their role in pregnancy loss. Dr. Laskin's research lab is one of three international core labs for this study, receiving plasma samples weekly from around the US and from our own patients, and testing them for coagulation proteins.

Look for more information, including expanded articles about LifeQuest's ongoing research initiatives, in future issues of our newsletter. ♦



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When it's time,
we're here.

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