

## HOW MANY IS TOO MANY? WHY RESPONSIBLE EMBRYO TRANSFER MAKES SENSE

### SO YOU WANT TO HAVE A BABY

When a woman is trying to conceive, and can't, nothing seems to spark the sharp pain of that experience more than the sight of two little babies, one swaddled in pink and the other in blue, nestled in a double stroller. "Two for the price of one." she might think. "Why shouldn't I do IVF once, conceive twins or triplets, get it over with, and live happily ever after?"



There are a number of reasons why that much coveted "happily ever after" often eludes patients who strive to get pregnant with more than one baby at a time. And if a healthy pregnancy, delivery, and baby is your goal, you should become aware of the potential risks to both yourself and your baby if you opt to consider pregnancy with twins or more.

### KEEPING YOUR EYE ON THE PRIZE

According to the Society for Assisted Reproductive Technology (SART), the objective of infertility treatment should be the birth of a single, healthy child<sup>1</sup> and for good reason. A multiple gestation, meaning twins or greater, can pose significant health risks. While these health concerns are not inevitable, they can include:

#### Complications to the Fetus from a Multiple Gestation:

- **Increased Rates of Miscarriage, Including (Preterm) Premature Rupture of Membranes (PPROM):** This occurs when the amniotic sac opens prior to the beginning of labor. PPRM before the 37th week of pregnancy can result in complications including stillbirth and premature birth.
- **Increased Rates of Death in-Utero or After Birth:** With singletons, this rate is 4.3 per 1,000 pregnancies but that rate increases to 15.5 per 1,000 for twins and 21 per 1,000 for triplets<sup>2</sup>. A single fetal demise of one twin occurs in up to 6.2% of all twin pregnancies<sup>3</sup> followed by considerable risk for the co-twin including increased risk of fetal loss, premature delivery, neurovascular injury and end-organ damage.
- **Cerebral Palsy:** Twin and triplet gestations cause greater stress on the mom during pregnancy and is a risk factor for cerebral palsy, particularly if one or more of the babies experiences fetal or infant death.
- **Discordance (Disparity) in Growth:** Discordance in fetal growth places twins and triplets at increased risk for several adverse perinatal outcomes, including preterm delivery and low birth weight<sup>4</sup>.

- **Twin to Twin Transfusion Syndrome (TTTS):** When twins or triplets share a placenta in-utero, TTTS may occur. This is caused by the formation of abnormal blood vessels. Instead of having a normal flow of blood between the babies, there is an unbalanced flow. This can cause one or more babies to receive too little blood and to experience low blood pressure, while the others may receive too much blood, and therefore experience high blood pressure<sup>5</sup>.

- **Vanishing Twin Syndrome:** This occurs when one of a twin/multiple gestation disappears in the uterus during pregnancy due to a miscarriage of one or more fetuses. The fetal tissue is reabsorbed by the remaining twin/multiple or the placenta.

- **Intrauterine Growth Restriction (IUGR):** This is defined as a fetal weight below the 10th percentile for gestational age as determined through an ultrasound. This can also be called small for gestational age (SGA) or fetal growth restriction<sup>6</sup>.

### **Complications to the Expectant Mom from a Multiple Gestation:**

- **Increased Levels of Nausea, Heartburn and Vomiting**

- **Increased Fatigue**

- **Iron Deficiency Anemia**

- **Pre-eclampsia (High Blood Pressure):** This is a medical condition in which hypertension arises during pregnancy, in conjunction with large amounts of protein in the urine.

- **Gestational Diabetes:** Women pregnant with twins or higher order multiples are more than twice as likely to experience gestational diabetes during their pregnancy. This may in part be caused by an increase in hormones produced by carrying an additional baby (or babies), which can interfere with the body's ability to process insulin.

- **Placenta Previa and Other Complications:** Whether there is a single, shared or multiple placentas, mothers of twins or more are at greater risk for complications such as placenta previa and placenta abruptio. Problems affecting the placenta can result in dangerous complications for the mom, including hemorrhage during pregnancy or after delivery. Fortunately, careful monitoring can detect most problems long before they pose a severe risk<sup>7</sup>.

- **Heart Problems, Including Heart Attack:** Women who carry two or more fetuses are thirteen times more likely to experience heart failure. Their risk of having a heart attack during pregnancy is nearly quadrupled<sup>8</sup>.

- **Incompetent Cervix:** In a typical pregnancy, the cervix remains closed. An incompetent cervix will painlessly begin to thin and widen, and unless corrected, can result in the loss of the baby or babies or a premature delivery.

- **Increased Need for Partial or Complete Bed Rest, and Limited Physical Activity:** Doctors will sometimes prescribe bed rest for expectant mothers of multiples in order to alleviate stress on the internal organs, and also, to let gravity support the stabilization of some underlying medical conditions<sup>9</sup>.

- **Emotional Issues:** Due to all of the increased risks inherent in a multiple gestation, expectant parents may unfortunately be faced with a painful decision about multifetal pregnancy reduction.

- **Pre Term Labor**

- **Increased Rate of Cesarean Section Delivery**

## **Complications After Birth from a Multiple Gestation:**

- Increased risk of infant death
- Need for Prolonged Hospitalization of Infant(s)
- Complications of Prematurity, including breathing problems such as apnea (temporary absence of breathing) and bradycardia (abnormally slow heartbeat).
- Intraventricular Hemorrhage (Cranial bleed) ranging from mild to severe
- Necrotizing Enterocolitis - a life threatening disease of the intestines.
- Complications Resulting from Hospitalization, including infections from breathing and feeding tubes and needles.
- Need for Blood Transfusions
- Retinopathy of Prematurity - significant eye problems.
- Hearing Problems such as full or partial deafness in one or both ears.
- Difficulty in Breastfeeding: This is of particular concern for infants born so prematurely that their suckling reflex has not as yet developed . These infants are unable to intake either breast milk or formula via suckling, and must be fed through a feeding tube inserted either through the mouth or nose.
- Increased Risk of Developmental Delays: Some minor developmental delays such as sensory integration disorders can often be greatly diminished or completely mitigated through early intervention.
- Increased Risk of Autism

## **Complications to the Family After Birth of a Multiple Gestation:**

- Financial Strain, particularly if one or more of the babies has special medical or developmental needs.
- Logistical Strain, such as managing work and child care, transportation, routine household tasks, and breast feeding.
- Emotional Strain, which can be exacerbated if the mother experiences long term post partum depression.

## **WHY RISK A MULTIPLE GESTATION? COULD IT BE THE COST MYTH?**

One of the rationales behind transferring large numbers of embryos is the patient's concern that only one or two In Vitro Fertilization (IVF) cycles will be an affordable option for them. Therefore, they opt to put all their eggs into one basket so to speak, and may encourage their physician to be more aggressive in their treatment. But it is important to keep in mind that aggressive and pro active are not the same thing. What if, instead, you opted to limit the number of embryos you wished your physician to transfer?

There's really good news about this option. Recent studies show<sup>10</sup> that elective single embryo transfer, meaning the transfer of only one embryo at a time, even when done with a frozen embryo, can actually be very successful. Studies also show that this option winds up being less expensive than a multiple embryo transfer. All this translates into results that are comparable in take home baby rates, with less money spent by the expectant parents.

And keep in mind, if your twins or triplets are born prematurely, or with health related issues, the resultant financial costs can quickly become astronomical.

## **GUIDELINES YOU CAN LIVE BY**

In 2009, The American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology (SART) co-published revised guidelines on the number of embryos that should be transferred during an IVF cycle for women. It is important to note this applies to IVF cycles where women are using their own eggs. For women undergoing egg donor IVF cycles, these guidelines apply to the age of the egg donor, not the age of the recipient.

**RECOMMENDED LIMITS ON THE NUMBERS OF EMBRYOS TO TRANSFER**

PROGNOSIS	AGE			
	<35 YRS	35-37 YRS	38-40 YRS	41-42 YRS
<b>Cleavage-stage embryos<sup>a</sup></b>				
Favorable <sup>b</sup>	1-2	2	3	5
All others	2	3	4	5
<b>Blastocysts<sup>a</sup></b>				
Favorable <sup>b</sup>	1	2	2	3
All others	2	2	3	3

<sup>a</sup>Justification for transferring one additional embryo more than the recommended limit should be clearly documented in the patient's medical record.  
<sup>b</sup>Favorable=first cycle of IVF, good embryo quality, excess embryos available for cryopreservation, or previous successful IVF cycle.  
*Practice Committee Number of Embryos transferred. Fertil Steril 2009.*

While exceptions to the guidelines are allowed, they should be limited and only considered in light of extraordinary medical circumstances. It is suggested that women discuss their particular situation with their reproductive endocrinologist and embryologist, and determine if the guidelines are applicable to their case.

While every woman's body is different, the risks associated with multiples can be very similar and affect women of all ages, weights, or overall health level.

Will every multiple birth result in terrible consequences? Thankfully, no. But are you willing to risk it in your own life? That is something you have to decide for yourself. The key may be to have a frank and honest discussion with both your reproductive endocrinologist and embryologist. Is elective single embryo transfer a good idea for you? Are the new ASRM/SART guidelines a better fit? Determine honestly what your support system will be like both during pregnancy and after birth, should you have twins or greater. Be proactive, knowledgeable and in control. That way you can proceed optimistically, and build towards creating the family of your dreams.

## END NOTES

- 1 Society for Assisted Reproductive Technology. "How Many Embryos Should I Have Transferred Back?" 26 January 2011. <<http://www.sart.org/detail.aspx?id=1919>>.
- 2 Ku, Lowell. 15 December 2010. <Internet Interview>.
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- 4 Davies, Margie, Denton, Jane, et al. "Information for Parents When Twins Share One Placenta". 26 January 2011. <<http://www.multiplebirths.org.uk/MC%20Pregnancy%20%20Version%2012%2017%205%2010.pdf>>.
- 5 American Pregnancy Association. "Intrauterine Growth Restriction (IUGR); Small for Gestational Age (SGA)." 23 January 2011. <<http://www.americanpregnancy.org/pregnancycomplications/iugr.htm>>.
- 6 Obstetrics and Gynecology. "Is Discordant Growth in Twins an Independent Risk Factor for Adverse Neonatal Outcome?" 20 January 2011. <[http://journals.lww.com/greenjournal/Fulltext/2004/01000/The\\_Effect\\_of\\_Birth\\_Weight\\_Discordance\\_on\\_Twin.13.aspx](http://journals.lww.com/greenjournal/Fulltext/2004/01000/The_Effect_of_Birth_Weight_Discordance_on_Twin.13.aspx)>.
- 7 Prindle Fiero, Pamela. About.com Twins & Multiples. "The Risks of Pregnancy with Twins or Multiples". 2 February 2011. <[http://multiples.about.com/od/pregnancy/a/pregnancyrisk\\_2.htm](http://multiples.about.com/od/pregnancy/a/pregnancyrisk_2.htm)>.
- 8 Ibid.
- 9 Tracy, Amy E. "The Pregnancy Bed Rest Book: A Survival Guide for Expectant Mothers and Their Families". (Berkley Publishing Group, New York). 15 January 2011.
- 10 Veleva Z, Karinen P, et al. "Elective single embryo transfer with cryopreservation improves the outcome and diminishes the costs of IVF/ICSI." 29 January 2011. <<http://www.ncbi.nlm.nih.gov/pubmed?term=elective%20single%20embryo%20transfer%20with%20cryopreservation%20improves%20the%20outcome>>.

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