Acacio
FERTILITY CENTER
Pathway to Parenthood

Joel Batzofin, M.D.
Laguna Niguel Office
27882 Forbes Road Suite #200 Laguna Niguel, CA 92677
Phone: (949) 249-9200 Fax: (949) 249-9203

Mission Viejo Office
26800 Crown Valley Parkway Suite, 560
Mission Viejo, CA 92691
Tel (949) 249 9200
Fax (949) 249 9203

Bakersfield Office
2225 19th Street
Bakersfield, CA 93301
Tel (661) 326-8066
Fax (661) 843-7706

EMBRYO TRANSFER ON DAY 3 VERSUS DAY 5: WHICH IS BEST FOR ME?

The concept of a day 5 or blastocyst transfer (BT) has been around for several years and is not new to the field of Assisted Reproduction. There have been reports of BT pregnancies in humans as early as 1990 and even earlier in animals. However the ability to consistently produce a high percentage of blastocysts from cultured embryos is a more recent development.

The freshly fertilized embryo is called a zygote. After the first 24 hours (Day 1), the embryo has divided into 2 cells. By Day 2, the embryo has 4 cells, and by the third day, there should be between 8-10 cells. Up to this point, embryonic development has been controlled by maternal genes in the oocyte. Around the 8 cell stage the embryonic genome is activated and the potential for further development is controlled by the embryo itself. By the fourth day, the embryo has 16-32 cells and is called a morula. Until now, all the cells have been the same. These "embryonic stem cells" are totipotent. This means that all cells contain all the information to make a complete human being. Removing a cell at this stage will not result in removing a leg for example. In other words, at this stage a single cell can be removed to look for genetic diseases without damaging the embryo. By Day 5, differentiation of the cells begins. A cavity forms in the center of the morula called the *blastocele*, which fills with fluid that will eventually become the amniotic fluid (the fluid surrounding the baby while in the uterus). The cells on the outside of the morula grow together and develop into the trophectoderm, which will eventually form the placenta and fetal membranes, while the cells on the inside of the morula group together to form the *inner cell mass*, which will eventually develop into the fetus. This complex creation is now called a blastocyst. As the blastocyst cavity fills with fluid, the blastocyst expands, thinning and eventually "hatching" from its enveloping "shell," the zona pellucida. The hatched blastocyst implants into the waiting endometrium on day 6 to 8 after ovulation.

Human embryos are very fastidious. They need specific metabolic requirements in order to survive. The earliest culture media were relatively simple in their composition and could only support limited embryonic development. The majority of embryos cultured in simple media could only survive to the third day of culture before undergoing a developmental arrest. Optimization of these simple media allowed reliable culture to the third day, which has been the standard day for embryo transfer for the last 8-10 years.

More recently, researchers in Australia, Scandinavia and in the U.S. simultaneously developed a new generation of culture media that reliably supports the growth of embryos to the fifth or sixth day. This development was based on the premise that the metabolic needs of the early embryo change as it moves through the fallopian tubes to the endometrial cavity and the new media are designed to mimic these environmental changes. Using "sequential culture systems," approximately 40% of "good quality" (7cells or more) day 3 embryos can be grown to the blastocyst stage and have made blastocyst culture feasible for many IVF programs. In fact, some programs exclusively use blastocyst transfers.

The inability to predict with certainty which embryos will successfully implant into the uterine lining still prompts some IVF practitioners, motivated with the desire to optimize IVF success rates, to transfer a large numbers of embryos at a time. While such practice indeed increases IVF pregnancy rates, it unfortunately also results in an unacceptably high incidence of multiple pregnancies, with devastating consequences to the resulting, often severely premature, newborn babies.

It has long been recognized that the more advanced the embryo's state and rate of development, the more likely it is to implant successfully into the uterine lining. It is also well established that "poor quality embryos" tend to divide (cleave) and develop more slowly, and are much more likely to arrest before reaching the blastocyst stage. It is therefore not surprising that researchers would focus on trying to grow embryos to the blastocyst stage in order identify "good quality embryos" that are more likely to implant successfully, by their ability to survive to the blastocyst stage of development.

It is important to note that in spite of the introduction of specialized culture media and new techniques for culturing blastocysts, it is still only possible to enable about 40% of "good quality" embryos to progress to blastocysts. However, since blastocysts are more likely to implant than are 3 day "good quality embryos," it is possible through the selective transfer of fewer blastocysts to improve IVF success rates while at the same time, significantly curtail the incidence of high-order multiple pregnancies (triplets or greater).

The uterus likely provides a better environment for embryos to flourish than the incubator in an IVF laboratory. Therefore, there has been a presumption that it would probably be best to transfer healthy embryos to the uterus sooner rather than later. Different IVF labs use different embryo grading systems to help select those embryos that will most likely implant. In reality, there is no definite answer to show day 3 versus day 5 transfer has a significant advantage. If PGD (preimplantation genetic diagnosis) is being performed, day 5 or 6 transfer is essential because the biopsy is done on day 3 or 5 and it takes time to get the results of the PGD. Outside of this, you should be guided by the usual practice of the clinic. At New York Fertility Services, we aim for a day 5 transfer when possible. We have a highly skilled embryology team and laboratory utilizing the latest technologies in embryo development.

Embryo Cryopreservation: At New York Fertility Services our practice is to cryopreserve (freeze and store) only those embryos that are deemed likely to survive the freeze/thaw and implant. In other words, we do not freeze embryos simply to say we have frozen embryos left over. Experience has taught us that allowing embryos to remain in culture for 2 – 3 extra days to ensure they will reach the blastocyst stage,

is a good method to select embryos worthy of being frozen. In other words, if an embryo does not reach the blastocyst stage of development, it more than likely will not survive the freeze thaw and almost certainly will not establish a pregnancy. In other words, all that would be accomplished would be to give a patient a false sense of security and generate a storage fee for the patients.

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This handout is intended as an aid to provide patients with general information. As science is rapidly evolving, some new information may not be presented here. It is not intended to replace or define evaluation and treatment by a physician.