

## ASSISTED HATCHING FACT SHEET

### Background

Hatching of the blastocyst is a critical process in natural embryo implantation. The "zona pellucida" is a protein coat that surrounds the egg and the early embryo not unlike an eggshell. Before the embryo can implant into the endometrium, the blastocyst must "hatch" out of the zona. Embryologists speculated that failure to hatch from the zona might be one reason for failed embryo implantation. In 1989, Cohen and associates published a paper claiming an increased implantation rate after mechanically weakening the zona just before transfer of embryos produced by in vitro fertilization. Since then, "assisted hatching" has become an important tool in the in vitro fertilization laboratory.

Assisted Hatching (AH) is performed by making a small incision in the zona pellucida surrounding the embryo. Embryologists use one of several techniques to make the zona incision. They may make a mechanical cut with a micro tool or "drill" a small opening with a chemical solution. Less commonly, they use a laser to cut a hole in the zona. At NCRS, we use a dilute acid solution called "Tyrode's". We perform assisted hatching on the day of embryo transfer. Embryos scheduled for cryopreservation (freezing) do not undergo assisted hatching though all day 3 frozen embryos do get assisted hatching after they are thawed for transfer. This is due to the likelihood that the freeze-thaw process artificially "hardens" the zona pellucida. To insure against exposing the embryo to potential attack by the maternal immune system, the recipient woman is prescribed a low dose of corticosteroid (Medrol) starting at retrieval and ending after transfer.

The implantation rate refers to the probability that an individual embryo will attach to the endometrial lining and develop into a pregnancy. There continues to be controversy about which patients might benefit from AH. Some studies have suggested that assisted hatching improves implantation rate in women over 40 years old, women with poor ovarian reserve and women whose embryos exhibit an unusually thick zona. In addition, the use of assisted hatching allows the embryologist to remove excess fragments from the embryo or improve the chance of hatching for embryos with thickened zonae. Some data suggests that removal of fragments may improve the implantation potential.

- Some studies show no benefit but they involve a general population.
- Most of the studies showing improved implantation involve specific populations such as multiple IVF failures, poor quality embryos or embryos with thick zonae.

Despite many years of experience with AH at many IVF centers, the true value and role of hatching remains controversial. We cannot guarantee improved pregnancy rates or that any pregnancy will result from using assisted hatching. Further, we cannot assure you that resulting pregnancies will be normal in course or outcome.

### Risks and Complications

1. There is potential for harm to occur to embryos during the hatching process. Although damage to the embryos is exceedingly rare, single cells within the embryo may be damaged in less than 1% of cases. Information available at this time indicates that this does not appear to affect the overall developmental potential of the embryo.
2. The exact likelihood of success for a given embryo or patient cannot be predicted. However, the implantation rate per embryo rises. This rise in implantation rate raises the risk for multiple gestation if more than one embryo is transferred.
3. Although unlikely, this technique may result in unknown risks to the fetus and/or mother. Given the higher implantation and delivery rates seen after assisted hatching of appropriately selected embryos, there is probably net benefit.
4. The corticosteroids given to the recipient are considered low dose. Over five thousand patients have now been treated with this regimen in cycles where there was some zona manipulation. The only notable side effect has been the more frequent occurrence of vaginal yeast infection. Though no side effects have been reported to date in these thousands of cases, the following are possible risks of corticosteroid use: new infection or masking of existing infection; increased blood pressure; fluid retention; electrolyte imbalance; mood swings; insomnia; depression; psychosis; muscle weakness; impaired wound healing; increased sweating; headache; vertigo; allergic reaction; loss of muscle mass; diarrhea; loss of appetite; rash; low platelet or red blood cell count.
5. There may be an increase in the occurrence of identical twinning after assisted hatching. Identical twins carry all of the risks of any multiple pregnancy as well as some exclusive to identical twins. These include premature labor and delivery, poor growth of one or both babies, tangling of the umbilical cords leading to intrauterine fetal death, "twin-twin" transfusion leading to discordant growth of the babies. While conjoined twins, a rare complication of identical twinning, have not been reported after assisted hatching, we cannot guarantee that this won't occur. Increased financial and emotional burdens may result from any of these events.