Information Sheet on Assisted Hatching of Embryos

Assisted hatching of embryos by micromanipulation has been advocated to help one particular group of patients who are having treatment with conventional in vitro fertilisation and embryo transfer (IVF-ET). These are couples who, every time they have a treatment cycle get apparently good quality embryos which, after transfer to the uterus, repeatedly do not result in a pregnancy or miscarriage. This particular situation is extremely frustrating to the patient, the clinician, and the scientists as everything seems to go well and yet the one stage of treatment over which we have little influence, i.e. implantation of the embryo onto the uterine endometrium, does not occur.

It has been postulated that a cause for this may be failure of the shell of the embryo, the *zona pellucida*, to rupture when it reaches the blastocyst stage, freeing the embryo to allow it to implant onto the uterus. Mechanisms for this potential failure are thought to include excessive hardening of the zona pellucida (a factor known to increase with age) and increased thickness of the zona pellucida.

In 1990 it was advocated by Professor Cohen at Cornell University in New York that the problem of failure of embryos to hatch from their zonae could be corrected by creating either a weakness or a hole in the zona. It is this practice that has become known as assisted hatching.

Methods of Assisted Hatching

Several approaches have been proposed to effect assisted hatching by creating a gap or weakness in the zona pellucida:

Chemical Zona Drilling - In this procedure an acidified culture medium is blown through a very fine needle onto one area of the zona, eroding a hole in it.

Mechanical Partial Zona Dissection - Here a fine needle is passed through part of the zona creating either a hole or an elongated slit in it.

Laser Zona Drilling - An extremely fine and controlled laser beam is used to drill a fine hole almost through the zona.

The Queensland Fertility Group uses a combination of laser dona drilling and mechanical partial zona dissection in its assisted embryo hatching programme . Fertility Gold Coast uses mechanical hatching.

Reported Success Rates for Assisted Hatching

For some years the only group reporting a consistent benefit from the procedure has been the New York group who originated it. Others have tested it on the following patient groups for whom it had been thought to possibly be of some help:

- Patients over 38 years of age.
- Patients who had received numerous transfers of good embryos without a pregnancy.
- Patients whose eggs had measurably thicker zonae.

No other study has found it to be of statistically significant benefit to these groups.

More recently an Israeli group has found it to be of benefit to a combination of two of these groups i.e. patients over 38 years of age with at least three embryo transfers without a pregnancy. QFG has implemented a similar programme for some years now and has results suggesting that this group does benefit slightly from assisted embryo hatching.

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Potential Problems

- *Pregnancy Rate*. For every study finding the procedure to be of some benefit there is another which has failed to detect any positive results.

In QFG's hands the procedure appears to restore to an almost normal level the pregnancy rate for a group of patients whose chances on routine IVF-ET were reduced due to age and other factors.

- *Embryo Damage*. Although this has never occurred in our hands it remains possible that the zona of an embryo or some of the blastomeres may be damaged during the procedure rendering the embryo non-viable.
- *Increased Risk of Multiple Pregnancies*. The procedure may result in a greater likelihood of identical twins to arise from one embryo and therefore a greater risk of a higher order multiple pregnancy from the transfer of several embryos.

Application

- Embryo hatching can be applied to any embryo being transferred after IVF, ICSI or thawing for frozen ET. It is not applicable to GIFT cases. It is not applied to embryos to be frozen as the hole in the zona will alter the dynamics of cryoprotectant penetration of the embryos.
- Assisted hatching is usually done on the second day after egg pick-up and insemination when the zona of the embryos can be breached or thinned without damage to the cells within the embryo. The embryo can be transferred at any time after the procedure.
- Assisted hatching is largely offered to that group of patients for whom it has been demonstrated to be of some help. Basic criteria for this group of patients include:
    - 38 years of age and over.
    - Previous failure to become pregnant following three embryo transfers of good to moderate quality embryos.
    - No history of any previous pregnancies at all.
    - Patients whose eggs/embryos show abnormal zona pellucida thickness.
- Assisted hatching has a further application in cases where pre-implantation genetic diagnosis (PGD) is to be done at the blastocyst stage. To ensure that the embryo hatches out for biopsy as early as possible, assisted hatching is done on them at day 2 of their development.

Costs

Assisted hatching uses the same staff, sophisticated equipment and fine hand-made tools as used for assisted fertilisation by microinjection. All that is missing is the sperm preparation and injection phase. As such the additional fee for assisted hatching will be $350 no matter what number of embryos are to be treated. This fee is NOT claimable upon Medicare or any private health insurance fund.

Summary

Assisted hatching is a procedure which has been around for many years and its best application is becoming more clearly established. It is not the magic "cure - all" that will help all IVF-ET patients but simply a procedure that may help a defined group of patients achieve normal IVF-ET pregnancy rates.