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Fact Sheet 1

Embryo Freezing

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The world's first live birth resulting from a frozen embryo occurred in Melbourne, Australia, back in 1984. Since then, embryo freezing has become an essential part of all IVF programs. Today approximately 50 to 70 percent of those undergoing IVF treatment will have embryo(s) to freeze and around 60 percent of all IVF births will result from the use of frozen embryos.

With tens of thousands of children born as a result of embryo freezing there is still no reported increase in birth defects in children conceived by frozen embryo(s) compared with children conceived naturally.

Why freeze embryos?

By freezing embryos and storing them for latter transfer we are increasing the *cumulative pregnancy rate*.

The *cumulative pregnancy* rate refers to the overall chance of a pregnancy resulting from a single stimulated IVF cycle utilizing all embryos obtained, both fresh and frozen.

For example, if six embryos are obtained from an IVF stimulation cycle, one or two can be transferred back on the stimulated cycle and the other four can potentially be frozen for later use. Not all embryos are suitable for freezing and all clinics have specific embryo freezing criteria. If no pregnancy results from the initial stimulated cycle, frozen embryos can be transferred back on subsequent cycles. Thereby the chance of at least one pregnancy from that initial stimulated cycle increases considerably.

If a pregnancy does result from the initial stimulated cycle, the frozen embryos can then be used in attempts at subsequent pregnancies in years to come.

The use of frozen embryos can therefore help reduce the need for stimulated IVF cycles, making treatment safer and more cost effective.

How long can a frozen embryo be kept?

From a biological perspective there appears to be no evidence to suggest that embryos deteriorate over time while in storage.

For the purposes of IVF treatment however, embryo freezing should be considered for short to medium term storage only.

The main benefits from frozen embryos are;

- If a pregnancy has not resulted from a stimulated IVF cycle, then the frozen embryo(s) are transferred on a subsequent menstrual cycle, avoiding the need for a further stimulated cycle.
- If a pregnancy has resulted from an IVF cycle, the frozen embryo(s) can be used following the birth of that child in an attempt to achieve another pregnancy without the need for a further stimulated IVF cycle.
- Where there is a need to store batches of embryos for later use, this process is called embryo banking. Examples would be if someone was about to undergo chemotherapy which may affect their future fertility they may wish to have embryos stored for later use, or if someone needs to have their embryos banked and genetically screened prior to embryo transfer.

Most States and Territories will have legislation governing the length of time frozen embryos can be kept for.

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For their part, IVF programs must provide clear information on the role of embryo freezing and the policies governing length of storage during the compulsory counseling sessions prior to the commencement of IVF treatment.

How is it done?

In order to cool embryos low enough to be stored in liquid nitrogen (-196 °C) techniques must be employed which will ensure that the embryo is protected against damage due to ice crystal formation during the freezing process. Currently there are two main techniques that can minimise potential freezing damage, slow freezing and vitrification.

Slow freezing involves the use of chemicals called cryoprotectants that minimise ice crystal formation (a bit like anti-freeze in your car's radiator) to potentially protect the embryo while it is slowly frozen down to -196 °C by specialised freezing machines. The process can take around 2 hours.

During the process of **vitrification** cryoprotectants are still used however the solution containing the embryo(s) is cooled so quickly that the water molecules do not have enough time to form ice crystals but rather instantly solidify into a solid "glass-like" structure, thereby significantly minimising potential damage to the embryo. This process takes just a few minutes to complete.

The thawing process is essentially just a reversal of the processes used for freezing the embryo. The embryos are exposed to diluted solutions of cryoprotectants and are returned to 37 °C.

Both freezing techniques are widely used around the world and have good success rates. Your treating IVF doctor will be able to explain which technique they use and their experience with it.

Transferring thawed embryos

A number of factors are taken into consideration when preparing to transfer a frozen embryo.

Timing of the embryo transfer

The embryo must be transferred into the uterine cavity at a time when the cavity lining, the endometrium, is receptive for the embryo to implant. This assessment is generally made by measuring hormone levels at various points in the transfer cycle as well as ultrasound measurement of the endometrial thickness.

Depending on the stage at which the embryo was frozen the clinical staff/embryologists can calculate the best time to transfer the embryo to obtain optimal pregnancy outcomes.

The type of menstrual cycle

There are primarily two types of menstrual cycles that can be used for transferring frozen embryos, a natural or an artificial cycle. Both have similar pregnancy rates and your IVF doctor will determine which is best suited for you clinical condition. The following describes both possible processes.

If your menstrual cycles are reliably regular and of average length (26-32 days) one option is to transfer the thawed embryo back on a **natural menstrual cycle** with no additional hormonal treatments being used. The menstrual cycle is monitored using either laboratory-based blood tests and/or home detection kits in conjunction with ultrasound monitoring of the ovaries and the endometrium. From this a time when natural ovulation has occurred can be determined and the appropriate time to transfer the thawed embryo can be calculated.

If a pregnancy does develop the advantage of this form of treatment cycle is that generally no additional hormonal therapy is needed during the pregnancy.

If your menstrual cycles are unreliable or irregular, for example in some women with polycystic ovaries or older women an **artificial cycle** may be used. Hormonal therapy is used to "override" the menstrual cycle. This will generally involve hormone replacement therapy in the form of an oestrogen during the first-half of the menstrual cycle and a progesterone during the second-half in order to induce an "ideal" menstrual cycle. As with the natural cycle described above, the level of hormones and the endometrial response to these hormones are monitored in order to calculate an ideal time for embryo transfer.

If a pregnancy does develop during an artificial thaw cycle the oestrogen and progesterone supplementation will generally need to be continued until the twelfth week of the pregnancy.

Success and outcome

There are many factors that will affect the success of both IVF treatment and frozen embryo transfer. Age, cause for subfertility, ovarian reserve and response to hormonal stimulation are to name but a few.

For most IVF clinics, frozen embryo transfer success rates are at least equal to, and in many cases higher, than those achieved for fresh embryo transfer during IVF stimulation cycles with fresh embryo transfer.

Recently, a number of large studies reported in the medical literature have suggested that not only may pregnancy rates be higher using frozen embryos but also the outcomes of these pregnancies may be better. Studies have shown that compared to pregnancies resulting from fresh embryo(s) transferred in a stimulation

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cycle, pregnancies resulting from the use of frozen embryos had a lower incidence of bleeding during pregnancy and resulted in fewer pre-term deliveries and less low-birth weight infants.

Many now believe that the endometrial lining is negatively impacted with the abnormally high hormone levels seen in IVF stimulation cycles resulting in these lower pregnancy rates and increased potential for pregnancy complications.

It is of little surprise then that many IVF clinics around the world are now moving away from the practice of transferring fresh embryo(s) to "freeze-all" programs where all embryos created and suitable for freezing are frozen for latter embryo transfer.

One thing appears certain; the importance of embryo freezing in IVF is only set to increase into the future.

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