

## ACT London Meeting 26<sup>th</sup> September 2018

### Speaker Gidon Lieberman Gynaecologist and IVF Consultant and Clinical Lead at Whittington Hospital

Based his presentation on the one he would give to a couple on their first visit. Covering the basics, with some extra detail, followed by questions. He stressed that in some areas viewpoints among his peers differed considerably and he was giving his view.

#### Basics

IVF initially developed to overcome tubal blockages and this is still what it does best (plus ICSI). Has been adapted to other conditions but not such a good solution eg PCOS and Endometriosis. Anovulation (mainly from PCOS) is the main cause of subfertility in the western world. Further subfertility problems are tubal blockage, endometriosis and male factors.

Categories of fertility treatment

1. Do nothing – have sex
2. Surgery
3. IVF technology
4. Donor
5. Surrogacy

**Natural IVF** (or natural modified). This is not really natural, the term relates to a non-stimulated cycle where various other drugs are given.

#### Long Protocol

Pituitary is switched off, inducing temporary menopause.

#### Short Protocol

Stimulation to make follicles grow but prevent ovulation. In a normal menstrual cycle 5-10 follicles grow in each ovary of which one becomes dominant and is released. All the others die off (undergo atresia). IVF is set up to mature all 10-20 follicles (in both ovaries) which are then collected for in vitro fertilisation.

A scan of a woman's ovaries can be used to determine the number of developing follicles (relating to AMH). In any month antral follicles will be detected which will develop to become the following month's maturing follicles, although only one will mature fully to be released during ovulation. This process may be prevented by the pill and in women with PCOS.

#### Stats

In any one cycle of IVF, a woman is less likely to have a baby than to have one.

#### Eggs and fertility

- A Female Foetus of 28 weeks gestation carries 6-7 Million eggs
- At birth this decreases to 2 Million
- At puberty 0.5M and of those only 1% will actually mature and be released.

**Best predictor of menopause** is one's own mother's menopausal history. A woman's fertile years will cease approximately 7 years before her menopause.

**Best predictors of fertility:**

- Age
- Time trying to conceive
- Age of mum when her youngest child was born, if she had unprotected sex. Or mum's menopause.

**Stress and Fertility**

From biomedical view then only significant in extreme circumstances e.g. drought. However, GL doesn't think it contributes to the destruction of ovarian tissue. It may influence the maturation of follicles (women stop ovulating and menstruating in extreme circumstances) or the uterine environment. Also people may stop having sex in some extreme circumstances.

**Toxins**

He doesn't think toxins are an issue in the short term. They may have more of an effect as a result of lifetime exposure (e.g. smoking, drugs, alcohol). He acknowledges that changes in the environment in the short term may affect chromosomal health and egg quality, but they are not considered a big factor in fertility clinics, GL hesitantly says that they may be a factor).

**DHEA**

Only one clinic in the world has shown a positive outcome using DHEA. It may help to produce more eggs, that is it may change the environment, but does not improve egg quality. There is no proven increase in life birth.

**Antral Follicle Count and AMH**

Ultrasound scans – often clinics charge more for antral follicle count, however GL says this is not justified as the counting of antral follicles does not require a special scan, it is simply the addition of counting these follicles (they look like black holes). AFC is just as good as AMH, so AMH probably superfluous.

**Sperm, ICSI and Fertility**

- Main indication is poor male factor or couples trying for extended period of time.
- In an IVF lab it is easier to do ICSI than IVF because the former tolerates more variation in lab conditions.
- ICSI can only be done with an egg that has expelled its first polar body.
- Risks associated with ICSI are related to poor sperm quality. If good quality sperm then not greater risk. It is possible that poor sperm could impact on male offspring.

- DNA Fragmentation tests – Gidon thinks it is ‘the biggest wallet opener in the world’. He has never seen it change the management of a single couple.
- If there are sperm issues – the man should go on an antioxidant diet for 8 weeks (the period of time it takes for sperm production).

## Embryology

In IVF the egg is mixed with about 100,000 sperm. In ICSI 1 sperm is selected and injected. In the USA ICSI is used mainly which is due to litigation factors rather than clinical outcomes.

If once sperm has entered the egg cell, the cell wall thickens and no further sperms can get in. In 2% of cases the sperm is fine, the egg is fine but no fertilisation takes place (possibly due to thick cell walls).

## Monitoring Embryos

This is Gidon’s view but opinions vary.

- Monitor embryo in the incubator **undisturbed** for 5 days (videoed 24/7) right through to blastocyst. The less disturbance the better.
- Egg has more influence than the sperm on embryo for first 3 days - so as a general rule, development problems during day 1-2 more likely to relate to the egg. Development problems during day 3-5 may be more likely due to a sperm problem.
- Gidon prefers not to give info on embryo grade to the couple as it is not straight forward to associate this information with life birth. 50% of ‘good’ blastocysts are (chromosomally) abnormal.
- Best outcomes are even cells and steady development.
- Important to look at the development right through because a fine looking blastocyst on day 5 may have shown unsteady development earlier and may not be viable (e.g. going from two cells to 3 instead of 4 on day 2).
- If embryos are not of good quality, Gidon prefers not to transfer as women are then more likely to blame their body for any failure.
- Gidon does not think there is any good evidence for the influence of Natural Killer cells or other immunological issues on fertility.

## If the pregnancy test is positive

- Rescan at 7 weeks – mainly to detect ectopic pregnancy which is higher risk in IVF than natural conception, and termination of an ectopic pregnancy is less dangerous at 7 weeks than later.
- The risk of miscarriage is the same for natural conception and IVF.

## IVF Risks

- To woman – OHSS and risks from surgery (e.g. puncture of the bladder or bowels or infection).

- To baby – 0.3% higher risk to child conceived with ICSI. There is also a risk of premature birth more often happening when twins are developing. Premature birth can cause problems later in life.
- IVF babies may have normal fertility, e.g. Louise Brown (first IVF baby) has had a child. However, in male offspring conceived with the help of ICSI due to sperm problems, there may be an inherited sperm quality factor.
- Difficult to know the effect on the baby of keeping embryos out of the body for 5 days. Could this impact on the offspring (of IVF babies themselves or offspring of IVF babies?).
- Overall IVF and ICSI seem to have very little effect on the health of the children.

### **Egg Freezing**

Only 6% chance of having baby from each frozen egg (normal chance of an unfrozen egg to develop into a baby is 10-16%).

In women/couples over 35 he would counsel them to try for baby rather than freezing eggs. Maybe good to freeze at younger age but can give false hope. More than double the chance with fresh eggs.

### **Embryo Freezing**

In general embryos survive the freezing process. So there is very good success and may be especially good for women with PCOS (and also if a woman develops OHSS).

### **NSAIDS**

NSAIDS drugs delay/inhibit ovulation. Their half-life is 5 days so shouldn't be taken for 5 days before ovulation.

Tranexamic acid for heavy periods with pain (can stop bleeding)

Mefenamic Acid for period pain without heavy flow but Gidon claims that other NSAIDs are just as effective.

**Watch this space. He will be back at some point to take things further!**

Minutes taken by Philippa Summers and Pia Huber