

Understanding the IVF Laboratory

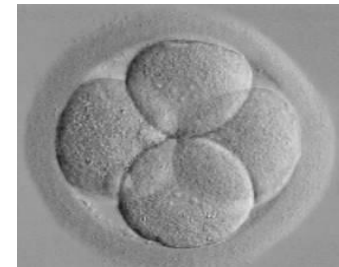
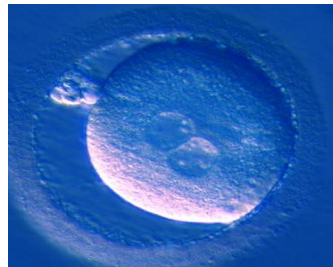
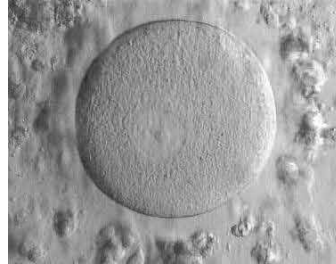
Marta Jansa Perez
Wolfson Fertility Centre

Fertility treatment options

- Follicular monitoring – timed intercourse
- Intra Uterine Insemination – partner or donor sperm
- IVF/ICSI
- Surrogacy
- Egg donation
- PGD/PGS
- Fertility preservation
 - medical or social

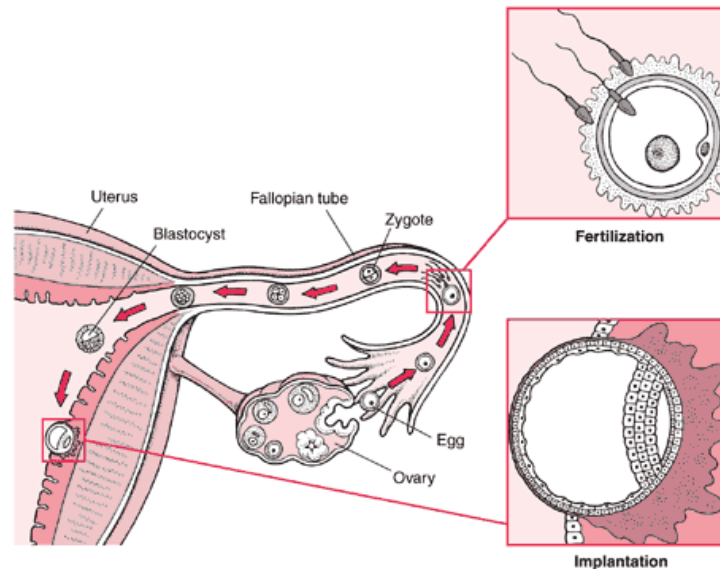


What does embryology involve?



Aims of the embryology laboratory

Creation of a large number of embryos and supporting their development in optimal conditions



Selection of the embryo/s with the highest implantation potential – tools?

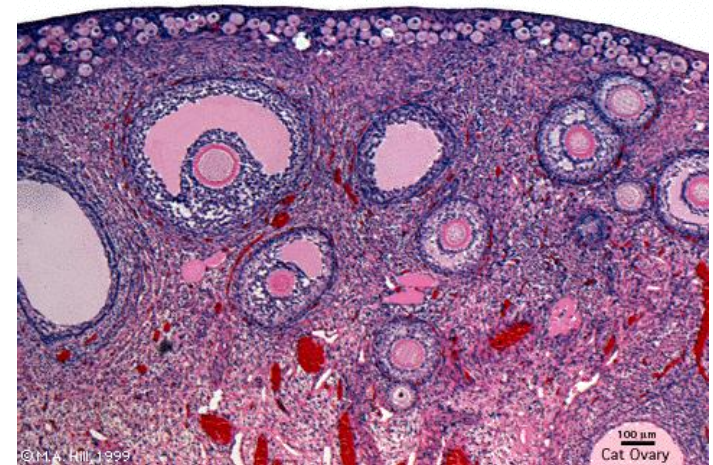


What can be controlled

- Stimulation protocols
- Lab environment; air quality requirements
- Culture conditions
- Gamete and embryo handling protocols

What can not be controlled

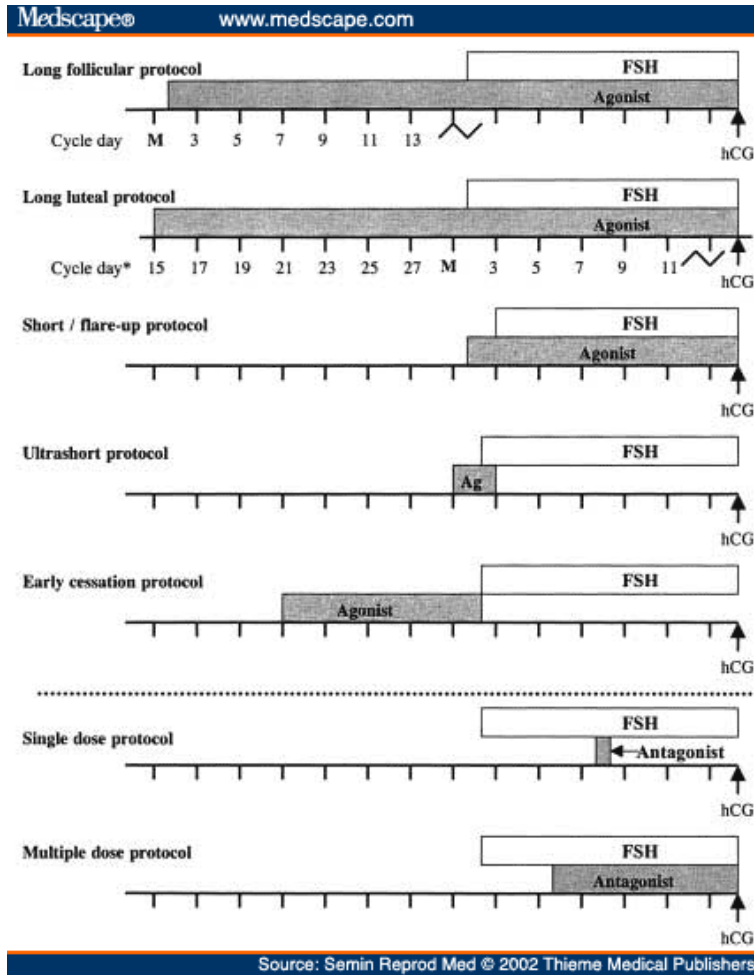
- Patient population: age, BMI, diagnosis
- Developmental potential of the eggs/embryos



The IVF/ICSI cycle

- **Egg collection (Day 0)**
- **Fertilisation (Day 1)**
- **Embryo culture (Day 1 - Day 6)**
- **Embryo Transfer (Day 2 or Day 3 or Day 5)**
- **Cryopreservation (Day 5 and/or Day 6)**

Gamete production - Oocytes



- Pituitary suppression (GnRH agonist)
- GnRH antagonist protocols
- Multifollicular development (FSH)
- Maturation (hCG/GnRH agonist)
- Oocyte recovery at 36-38hrs post trigger



Sperm analysis parameters- what is normal?

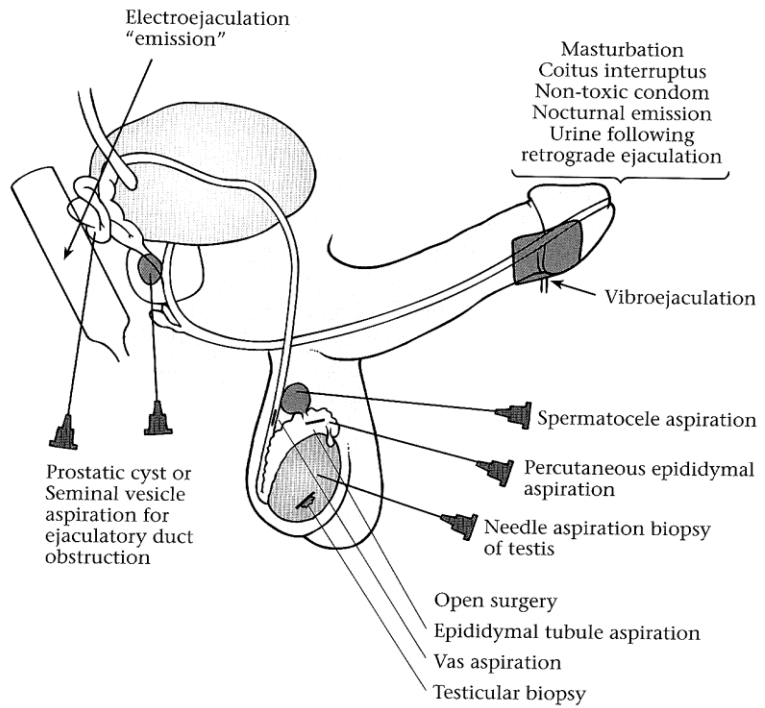
World Health Organization reference values:

- semen volume: **1.5 ml or more**
- pH: 7.2 or more
- sperm concentration: **15 million spermatozoa per ml or more**
- total sperm number: 39 million spermatozoa per ejaculate or more
- total motility (percentage of progressive motility and non-progressive motility): **40% or more motile or 32% or more with progressive motility**
- vitality: 58% or more live spermatozoa
- sperm morphology (percentage of normal forms): **4% or more**

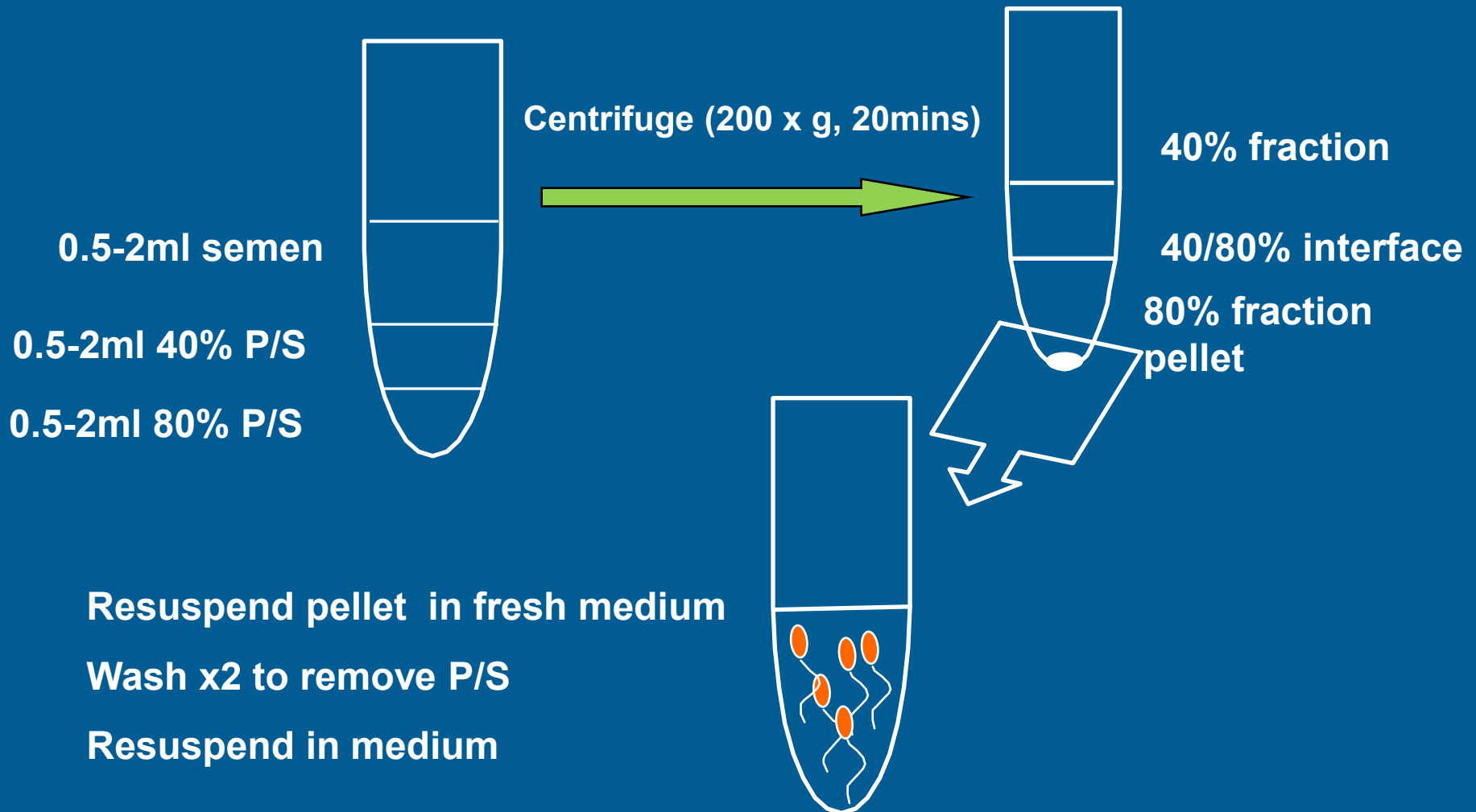
[Fertility (NICE guideline CG156), recommendation 1.3.1.1]

Normal values are based on data from men with proven fertility, men who were known to help their partners conceive in the previous 12 months

Sperm



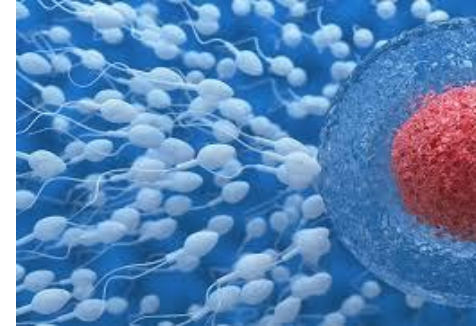
Concentrating motile sperm



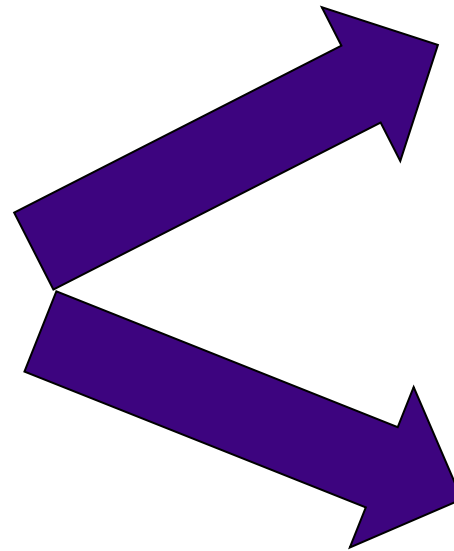
IVF / ICSI Treatment Cycle



**Egg Collection
+
Sperm Analysis
and Preparation**



**IVF Insemination
OR
IntraCyttoplasmic
Sperm Injection**

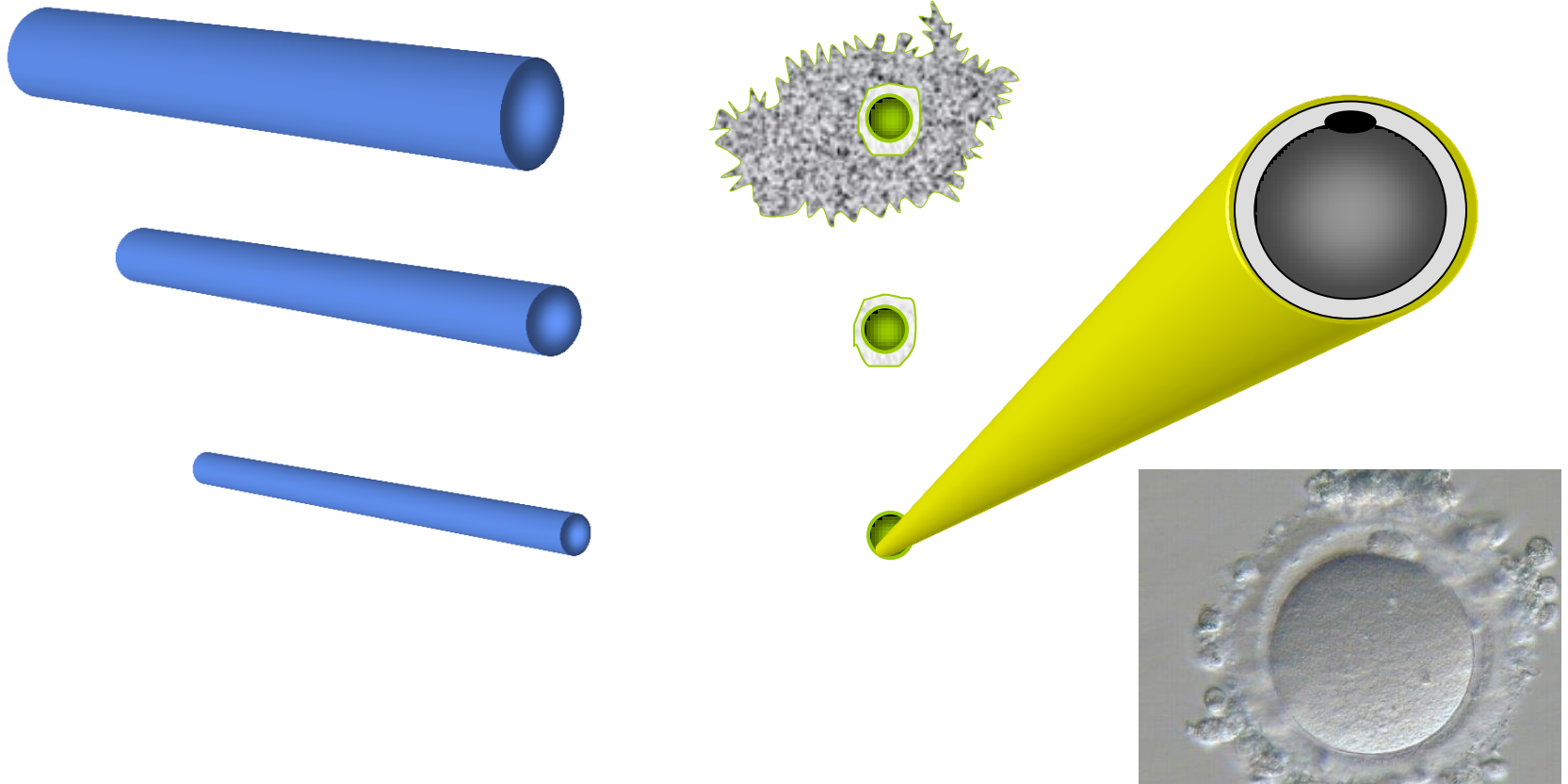


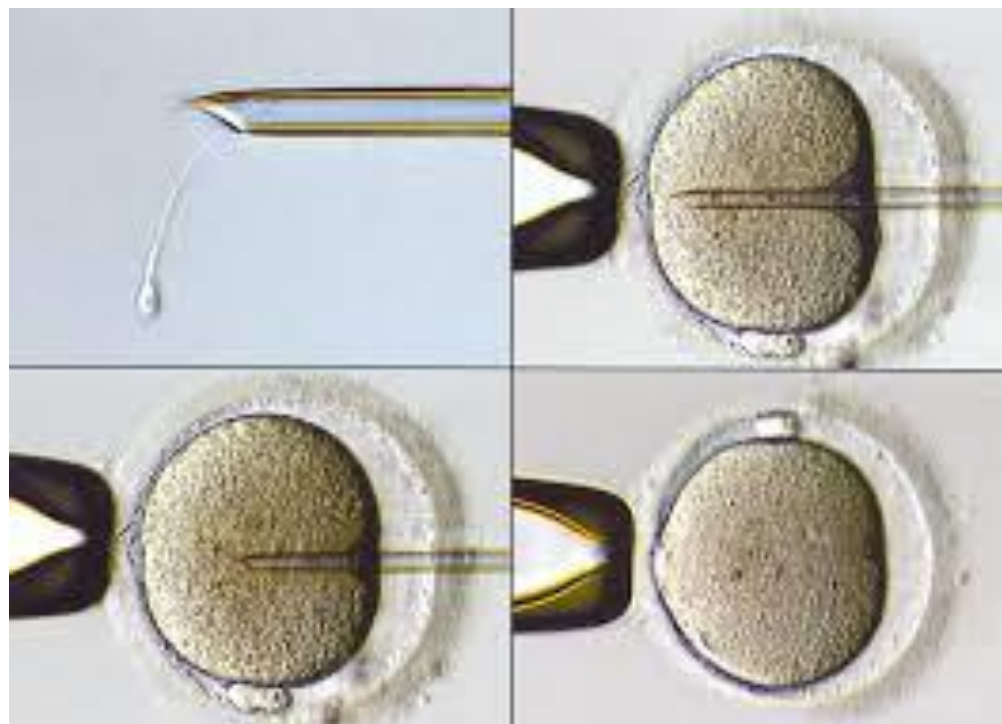
**Depending on sperm
parameters and
patients' history**



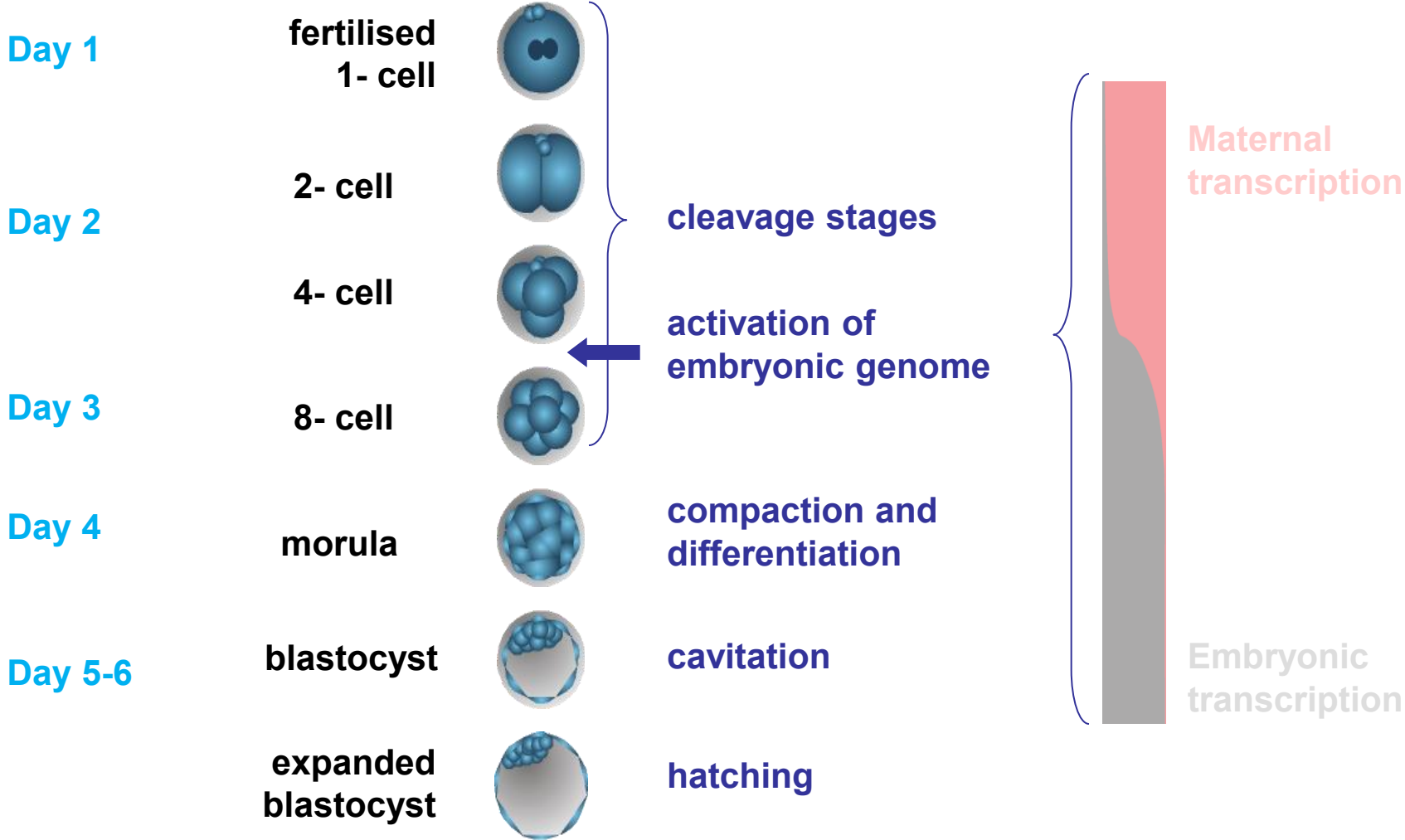
ICSI

Oocyte denudation – removal of cumulus cells by cumulase and mechanical action

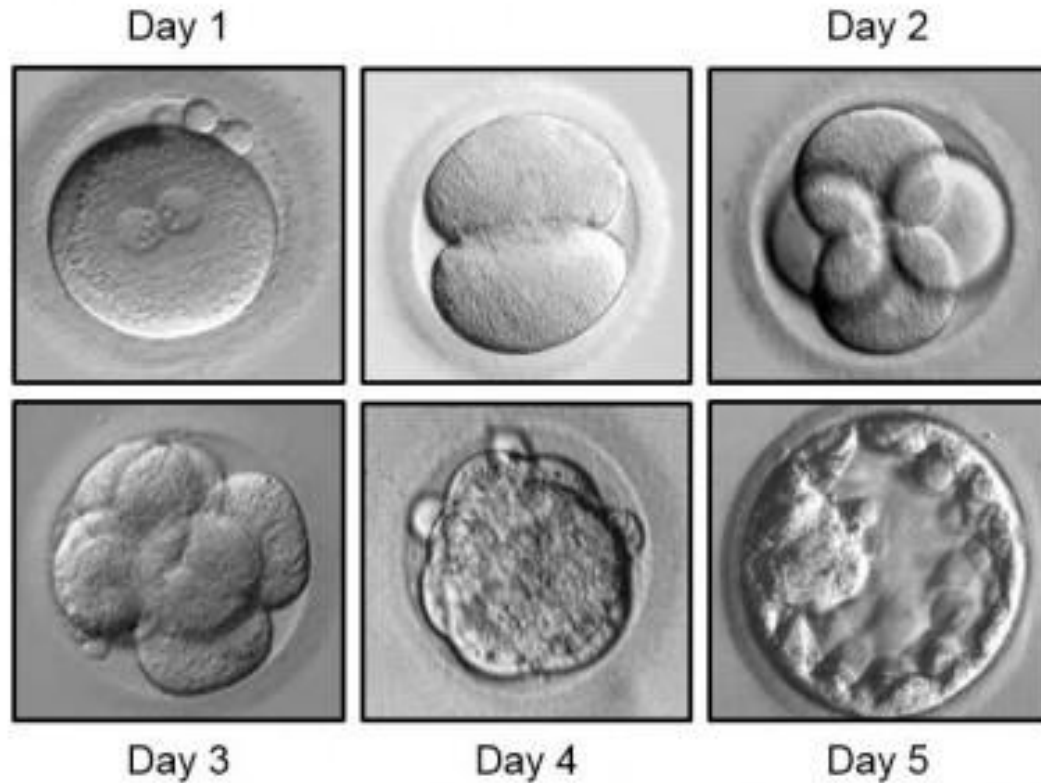




After Fertilisation



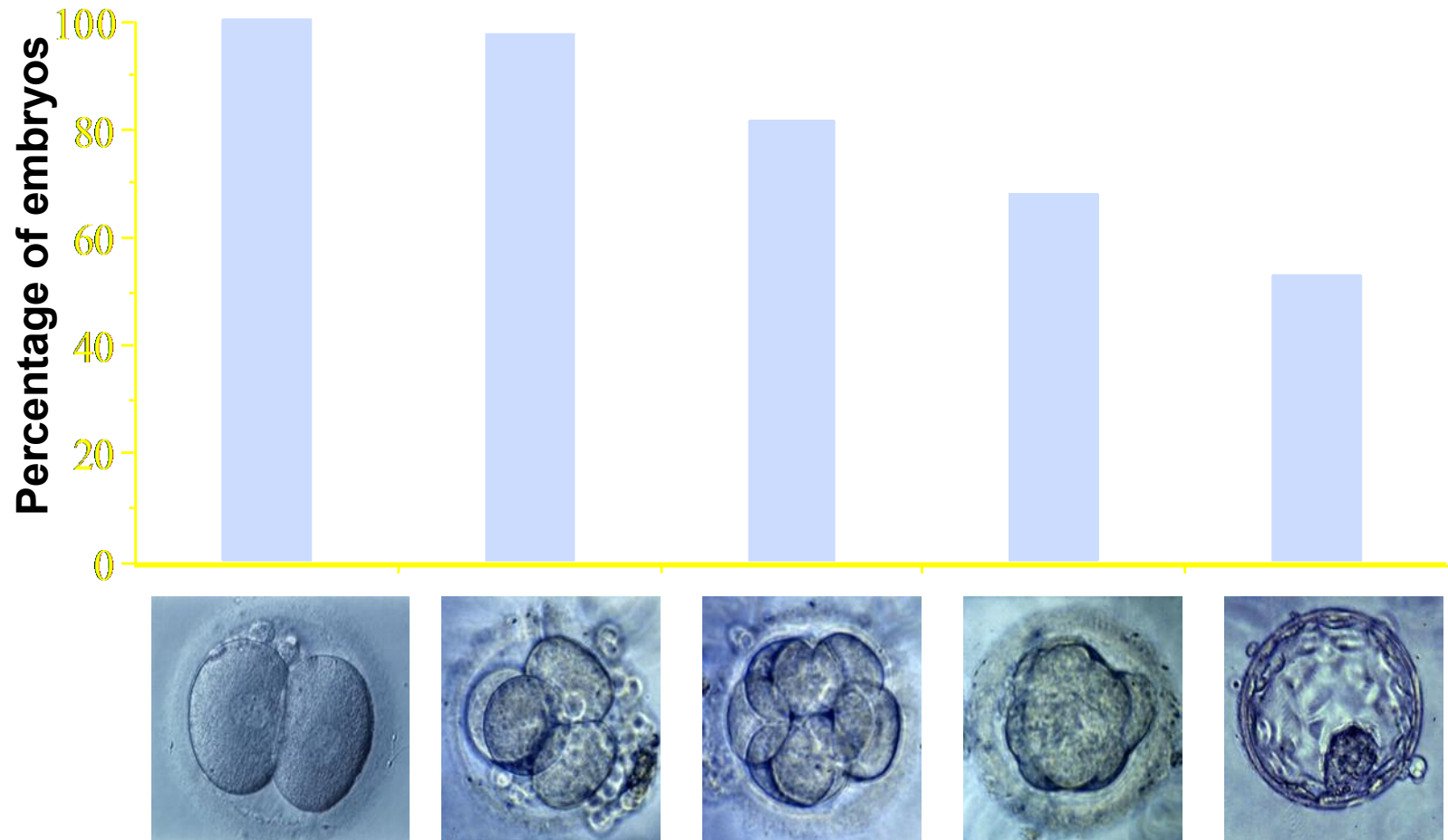
Embryo Development



Embryo Development

Using time lapse videos you can see an embryo develop from fertilisation stage (Day 1) to the blastocyst stage (Day 5)

Human embryo arrest *in vitro*



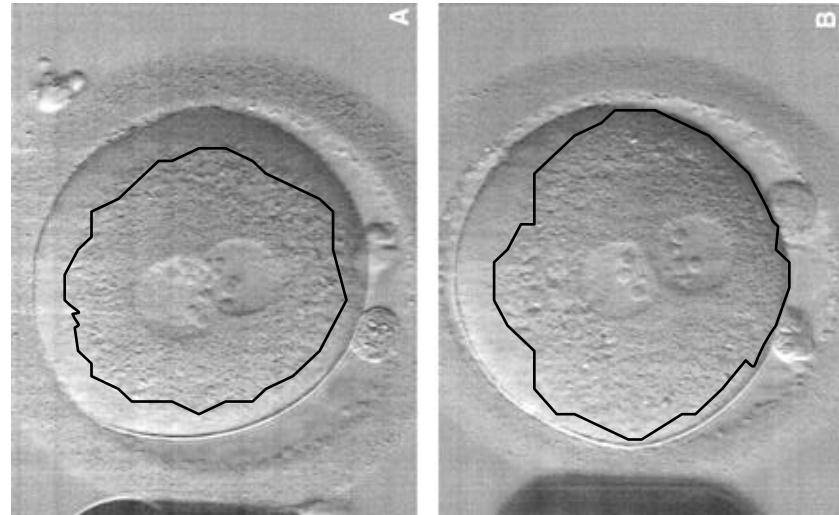
Choosing embryos – embryo morphology

•Zygotes

- Pronuclear scoring
- Syngamy/ early cleavage

•Embryos

- Developmental rate
- Cell shape/ size
- Fragmentation
- Multinucleation



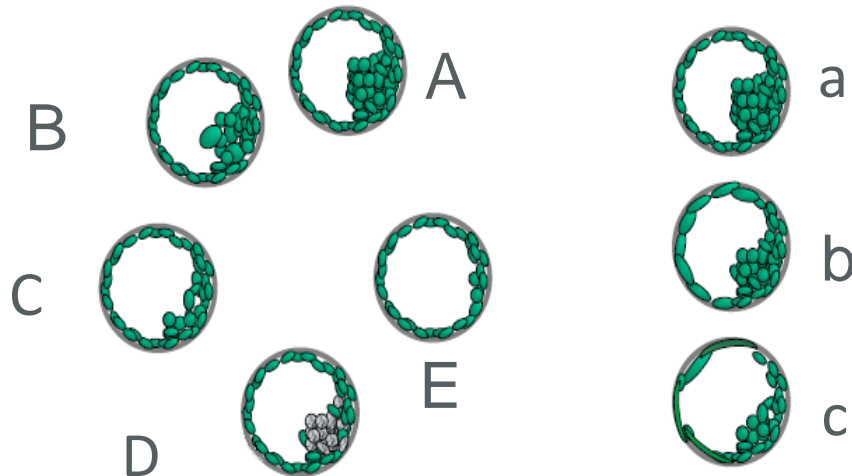
•Blastocyst formation

- Presence of trophectoderm
- Presence of Inner Cell Mass

Blastocysts

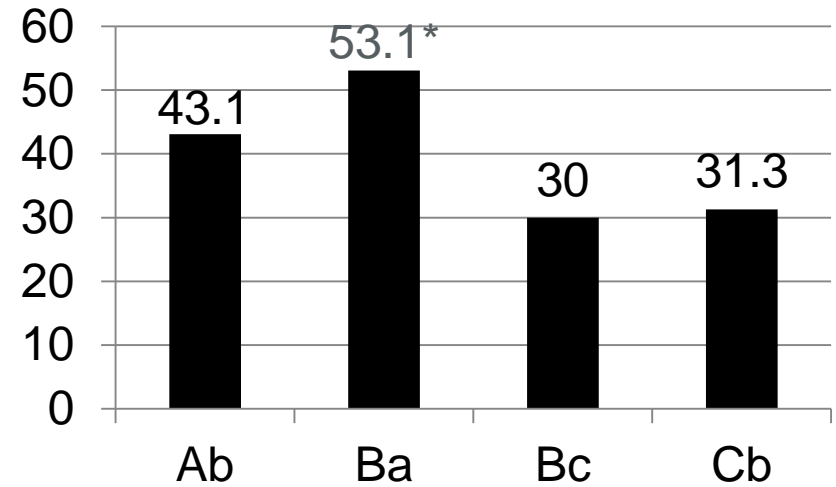
Inner Cell Mass

Trophectoderm



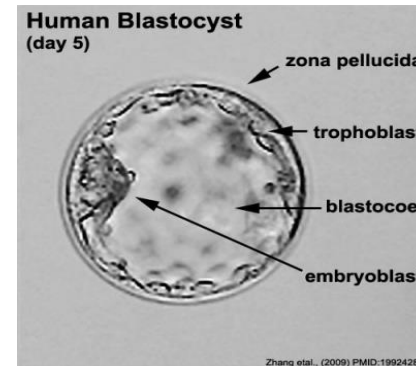
Trophectoderm or Inner Cell Mass Grade – which has a greater influence on embryo implantation?

Implantation rate



Embryo Transfer

- Is carried out either on Day 2, 3 or 5 of embryo development depending on number and quality of embryos
- Blastocyst culture (to day 5) is offered for better selection of the best embryo(s) for transfer
- Discussion with embryologist on day of transfer about embryo quality and embryo(s) for transfer or potential cryopreservation

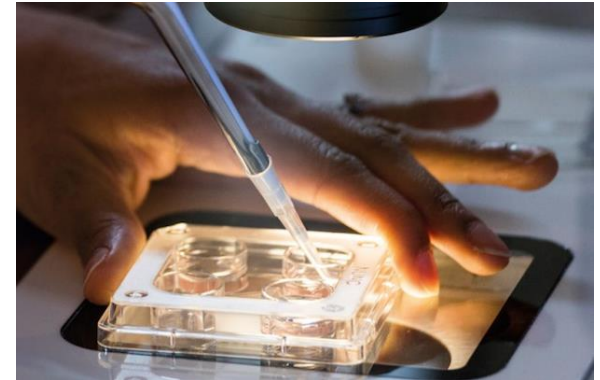


Single Embryo Transfer Policy

Current national drive by HFEA to reduce the number of twin pregnancies

We recommend a single embryo transfer in the first cycle for patients <37 yrs with good quality embryos (53% CPR)

Some CCGs will insist on this as a condition of funding

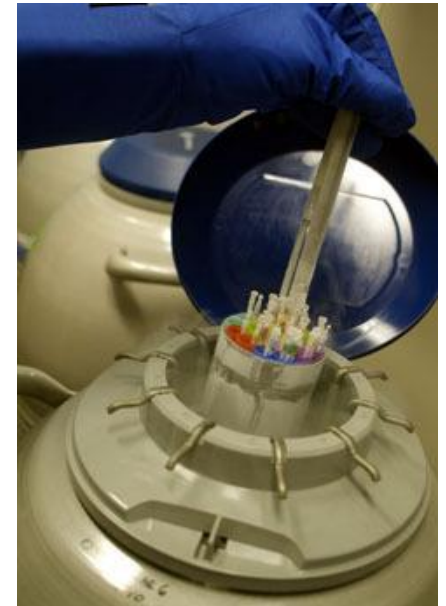
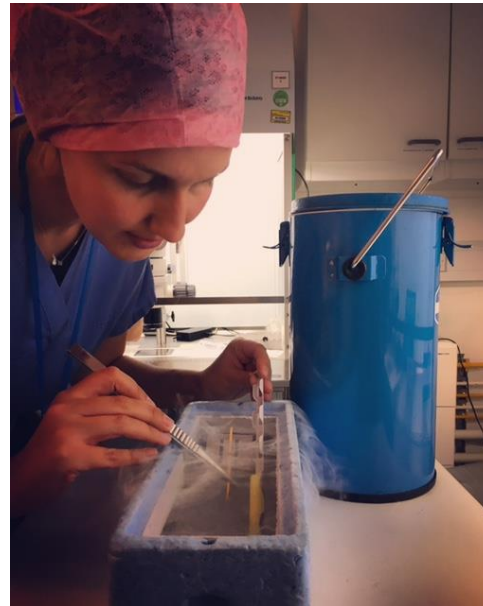


Embryo Cryopreservation

Use the advanced technique of Vitrification to cryopreserve surplus, good quality embryos for future use

Can also vitrify eggs if required

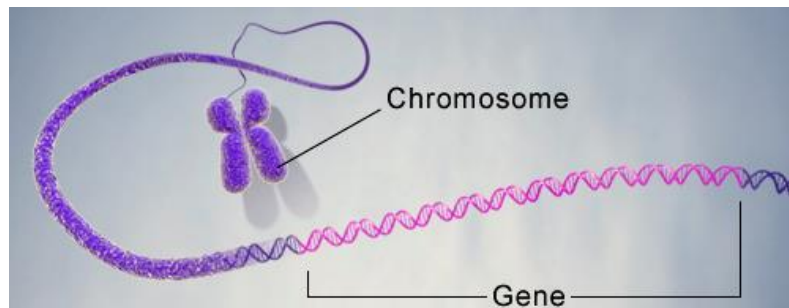
Improved success rates from older methods (called slow freezing)



PGD/PGS

Testing of embryos using:

- **PGD for specific genetic disorders - HFEA licence for each condition**
- **PGS screening for aneuploidies**



The IVF laboratory



The IVF Laboratory Employing the Latest Technology

HFEA fully accredited laboratories



Modern laboratory- Refurbishment
and new lab equipment in January
2017



Enhanced confidence with RI
Witness™ - electronic witnessing
system



RI WITNESS™

The Embryology team

- **Embryologists: Healthcare Scientists (also known as clinical scientists). Perform diagnostic services and therapeutic embryological procedures**
- **Training and monitoring of performance in accordance to National standards**
- **Continuous Quality Control**
- **Communication with the patients**



Requirements for all UK IVF units

- **Inspection/ licensing of establishments by competent authority - HFEA in UK**
- **Quality management system**
- **Ensure that all staff were properly trained**
- **Audit**
- **Key Performance Indicators (KPIs)**

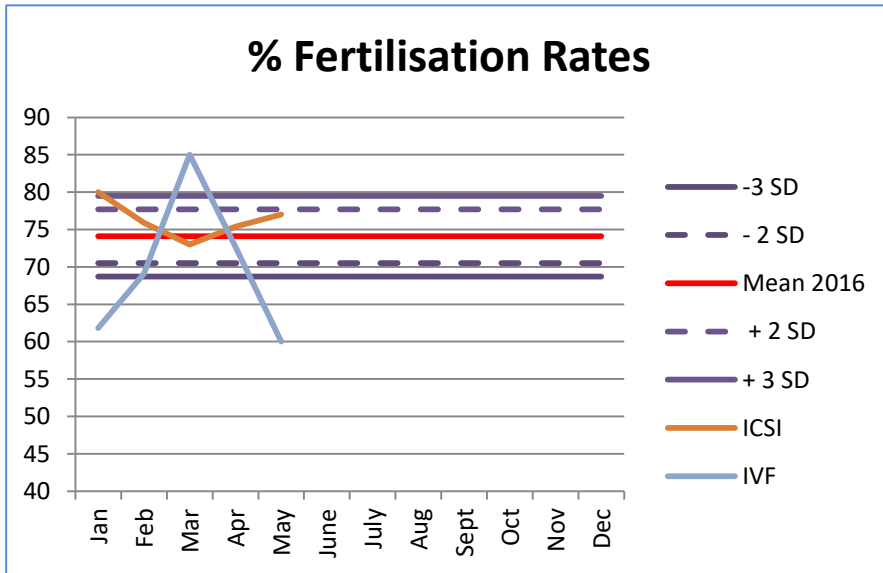


Laboratory specific requirements

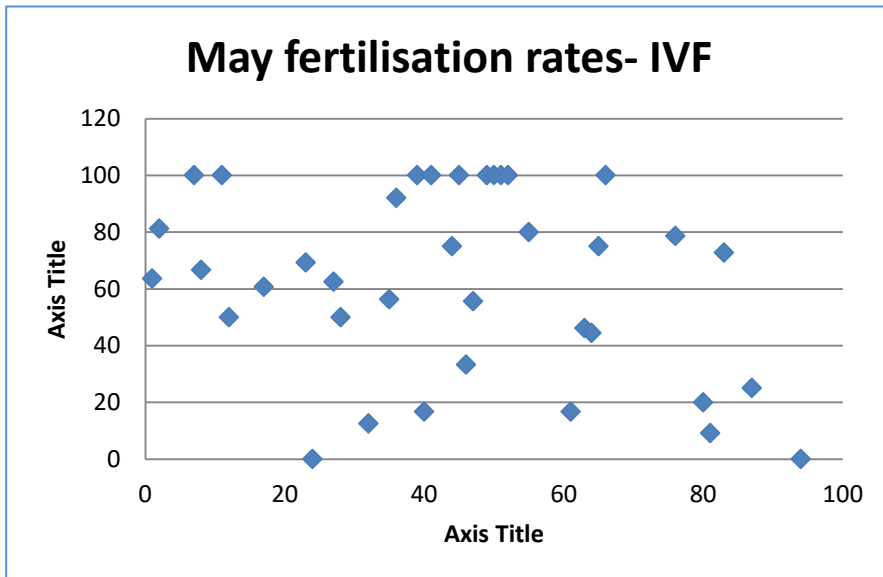
- **Traceability of cells/tissues –batch control**
- **Monitoring adverse incidents or reactions**
- **System of regulating imports and exports from and to other countries to ensure their safety and quality**
- **Air quality- Grade A processing/ Grade D background**

Monitoring system for all critical laboratory equipment

The screenshot displays the ViGIE monitoring system interface. The main area features a line graph titled "PINK 1 L Temp" for the "IVF | IVF&CSI LAB". The y-axis represents "Temperature" in degrees Celsius, ranging from 35.80 to 37.40. The x-axis shows time from 13/07, 14:07 to 14/07, 14:57. The graph shows a stable temperature around 37.10°C with minor fluctuations. Below the graph, a summary bar displays the current temperature as 37.10°C (2017-07-14 14:57:08), along with minimum (36.00°C), average (37.10°C), and maximum (37.10°C) values. The right sidebar lists various equipment items: PINK 1 Contactor, PINK 1 L Temp (highlighted), PINK 1 R Temp, PINK 2 Contactor, PINK 2 L Temp, PINK 2 R Temp, PINK 3 Contactor, PINK 3 L Temp, and PINK 3 R Temp. The bottom of the interface includes a footer with "Tutorial ViGIE 2.6 - Help Manual - Support contacts", social media icons, and a taskbar with open applications like "Introduction to cli...", "ViGIE Solutions - ...", "IDEAS V5.3", "Understanding th...", "WFC Open Evenin...", and "Inbox - Marta.Jan...".



FR 2017	Mean 2016	ICSI	IVF	Benchmark
Jan	74.1	80	61.8	65
Feb	74.1	75.9	69.1	65
Mar	74.1	73	85	65
Apr	74.1	75.4	72.7	65
May	74.1	77.0	60	65
June	74.1			
July	74.1			
Aug	74.1			
Sept	74.1			
Oct	74.1			
Nov	74.1			
Dec	74.1			



Changes in lab:

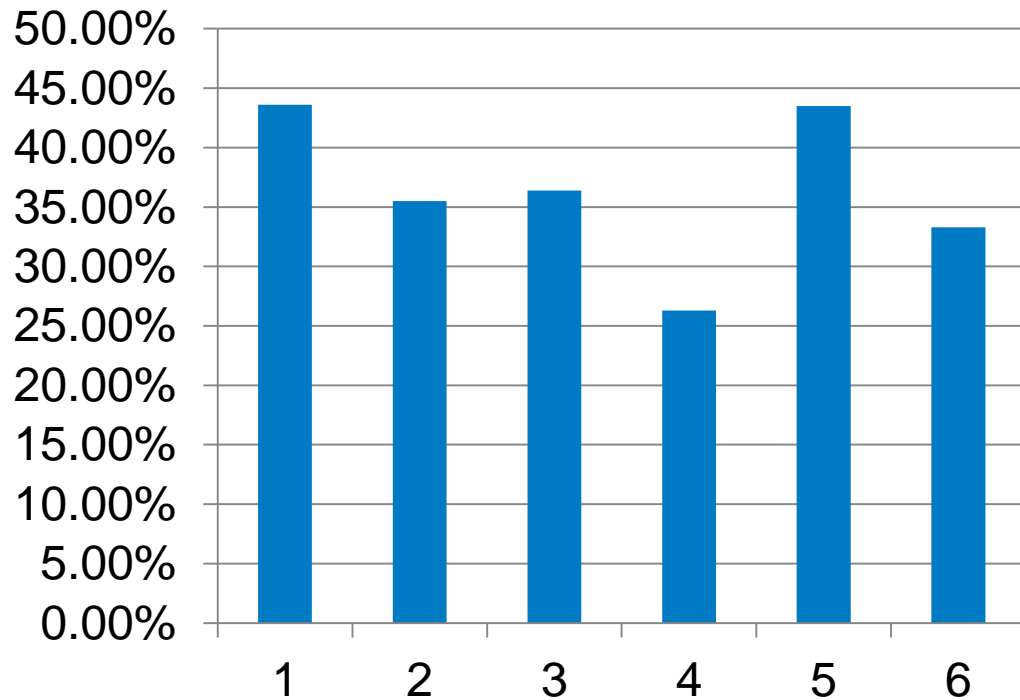
31/05/2017- Storing Puresperm back into fridge immediately after aliquoting

Previous practice- to leave bottle out for prolonged periods of time.

31/05/2017- Converting patients with any previous abnormal semen analysis to ICSI.

June Fertilisation Rates= 80% (2pn/MII)

ICSI CPR/Embryologist 2017



	#	CPR
1	55	43.6%
2	31	35.5%
3	33	36.4%
4	38	26.3%
5	23	43.5%
6	12	33.3%

Embryologist 4 June 2/6

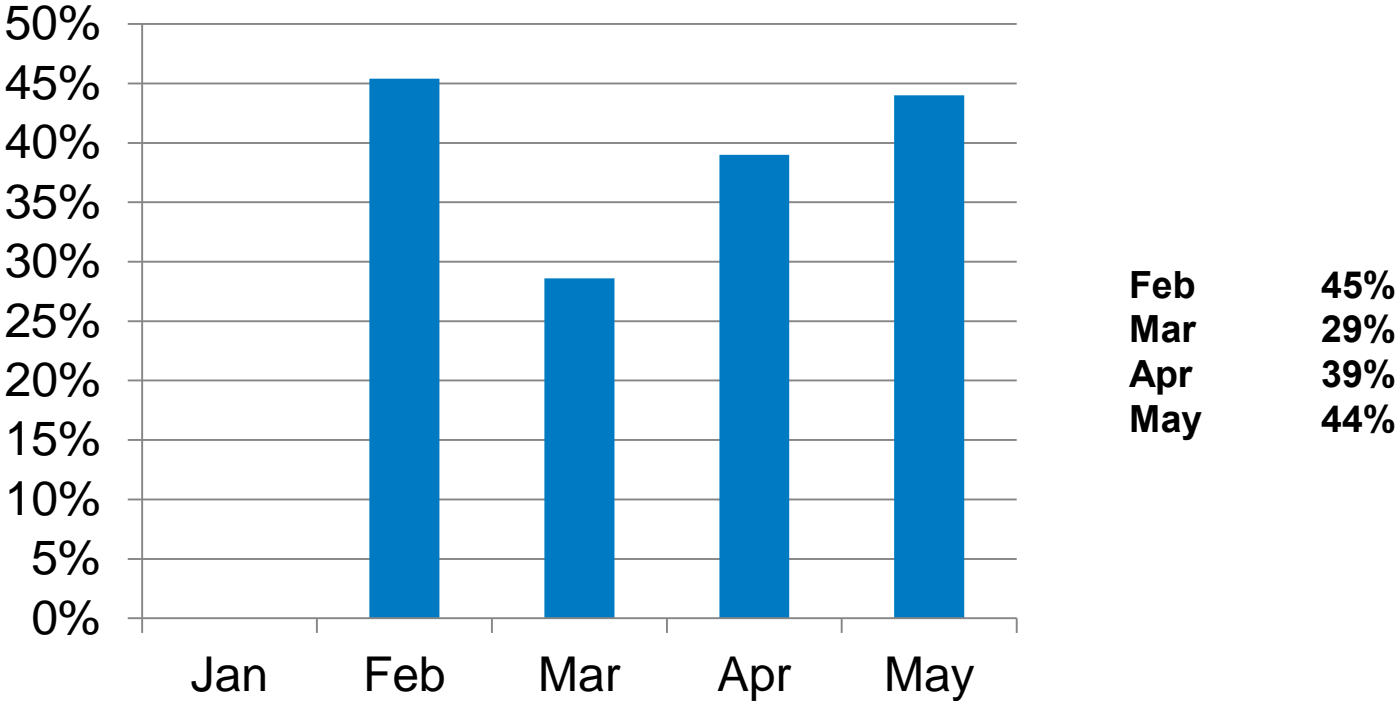
Recent Results Fresh IVF/ICSI April-May 2017

Clinical pregnancy rate per embryo transfer **44%**

June biochemical pregnancy rate **54%**



CPR FERC ET 2017



Research

- **Low responders IVF/ICSI**
- **Group vs individual embryo culture**
- **Morphokinetics and testicular sperm**
- **HABSelect trial**
- **E-freeze trial**
- **Metabolomics**

E-Freeze

To determine if a policy of freezing created embryos, followed by thawed frozen embryo transfer is a more **clinically** effective, **safer** and **cost effective** way to provide in-vitro fertilization when compared with the current practice of transferring fresh embryos.

Primary Outcome

- **Healthy baby rate:**
 - Term
 - Singleton
 - Live birth
 - Appropriate weight for gestation



Thank you

