A review of factors influencing the implantation of euploid blastocysts after in vitro fertilization

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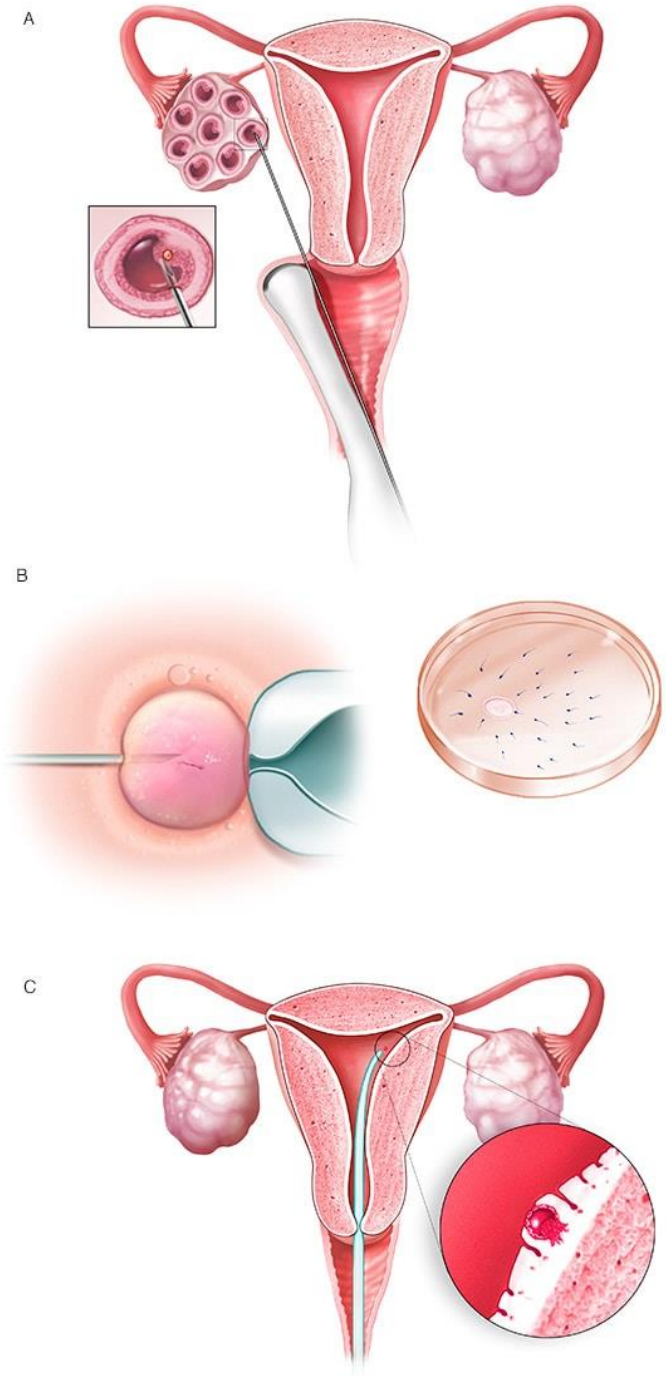
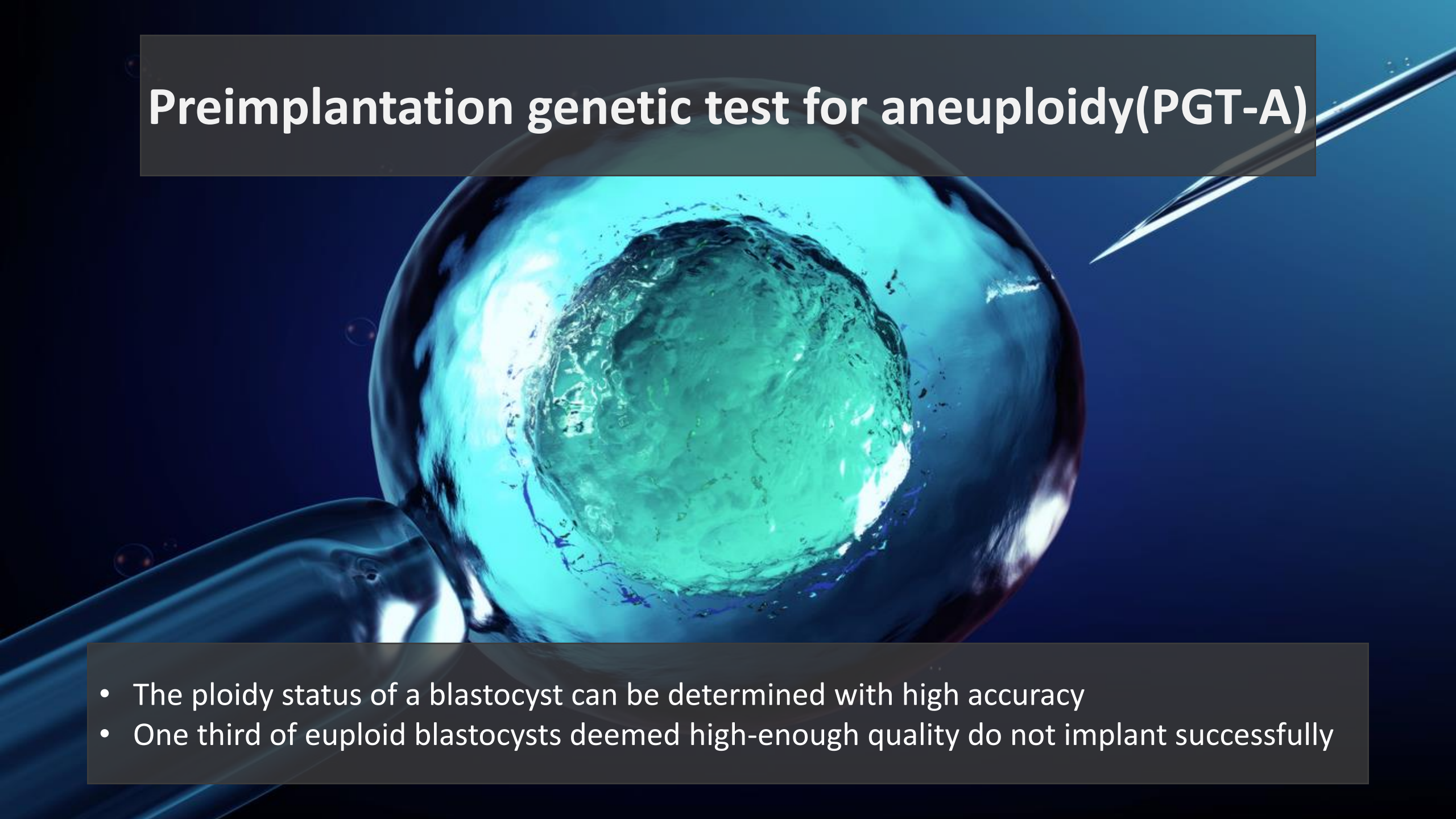


In Vitro Fertilization(IVF)

- Successful implantation of an embryo into a receptive endometrium

- Implantation factor
  - **Embryo quality**
  - Endometrial receptivity
  - Embryo transfer technique

Preimplantation genetic test for aneuploidy(PGT-A)



- The ploidy status of a blastocyst can be determined with high accuracy
- One third of euploid blastocysts deemed high-enough quality do not implant successfully

TABLE 1

Summary of evidence by subcategory for factors influencing implantation of euploid blastocysts.

Category	Subcategory	Summary statement
Embryonic factors	Blastocyst morphology	There is fair evidence to suggest that an increasing morphological grade of the ICM and trophectoderm has a positive impact on the implantation potential of euploid blastocysts.
	Blastocyst expansion stage	There is fair evidence that nonfully hatched euploid blastocysts have a higher chance of implantation than fully hatched euploid blastocysts.
	Timing of blastocyst formation	There is fair evidence that the implantation rates of euploid day 7 blastocysts are lower than those of day 5 and 6 euploid blastocysts.
	Mitochondrial DNA	There is insufficient evidence to determine whether testing mitochondrial DNA content in euploid blastocysts has an impact on the implantation potential.
Uterine factors	Endometrial appearance	There is insufficient evidence to determine whether endometrial compaction after the start of progesterone in embryo transfer cycles impacts the implantation potential of euploid blastocysts.
	Endometritis	There is fair evidence that the treatment of chronic endometritis can increase the likelihood of successful implantation in patients with a history of recurrent implantation failure, although further studies are needed in euploid blastocysts.
	History of cesarean section	There is fair evidence that a history of a prior cesarean lowers the implantation rate of euploid blastocysts after single embryo transfer.
	Presence of adenomyosis and endometriosis	There is insufficient evidence to suggest whether the presence of adenomyosis or endometriosis impacts the implantation of euploid blastocysts.
	Arcuate uterus	There is fair evidence that a diagnosis of an arcuate uterus does not impact the implantation rate of euploid blastocysts.
	Ease of transfer	There is fair evidence that a difficult embryo transfer does not lower the implantation rate of euploid blastocysts.
	Endometrial disruption	There is fair evidence that endometrial disruption before the transfer of a single euploid embryo does not improve the implantation rates.
IVF protocols	Ovarian stimulation and trigger	There is fair evidence that ovarian stimulation and trigger type do not impact the implantation rate of euploid blastocysts.
	FET protocols	There is good evidence that the type of FET preparation protocol does not impact the implantation rate of euploid blastocysts.
	Timing of transfer	There is insufficient evidence to determine whether adjusting the timing of the embryo transfer based on endometrial receptivity testing impacts the implantation rate of euploid blastocysts.
	Progesterone level	There is fair evidence to suggest that the implantation of euploid blastocysts is improved when the progesterone level is >20 ng/mL on the day of embryo transfer.
	Being from a previously vitrified egg	There is insufficient evidence to determine whether the implantation rates are altered if euploid blastocysts are derived from previously vitrified oocytes.
	Fresh vs. frozen transfer	There is fair evidence to suggest an improvement in the implantation rates of vitrified-warmed blastocysts compared with those of fresh blastocysts.

Embryonic factor

Uterine factor

IVF protocols

Patient factor

Embryology protocols

		blastocysts compared with those of fresh blastocysts.
Patient factors	Maternal age	There is fair evidence that extremes of maternal age can negatively impact the implantation potential of euploid blastocysts.
	Paternal age	There is fair evidence to support that an advanced paternal age of 41–50 years impacts the fertilization rates but not the implantation or clinical pregnancy rates of euploid blastocysts.
	Sperm DNA fragmentation	There is fair evidence to suggest that sperm DNA fragmentation index does not impact the euploidy rates or pregnancy outcomes.
	BMI	There is good evidence that an increased maternal BMI leads to worse pregnancy outcomes after the transfer of euploid blastocysts, including increased miscarriage rates and decreased live birth rates.
	MTHFR gene mutation	There is fair evidence to suggest that MTHFR homozygosity in euploid blastocysts may negatively impact the implantation rates.
	Vitamin D level	There is fair evidence that low vitamin D levels do not negatively impact pregnancy outcomes in patients undergoing euploid blastocyst transfer.
	TSH	There is fair evidence that the TSH levels of <2.5 mIU/L do not impact pregnancy outcomes after a euploid blastocyst transfer.
Embryology protocols	Timing of embryo biopsy	There is good evidence that cleavage-stage biopsy negatively impacts the euploid embryo clinical pregnancy rate, whereas blastocyst-stage biopsy does not appear to have the same negative impact.
	Size of biopsy	There is fair evidence that a larger biopsy size can negatively impact the euploid embryo pregnancy rates.
	Type of culture media	There is good evidence that culturing euploid blastocysts in sequential media over monophasic media does not improve the implantation rates, although blastocyst progression is improved.
	Culture temperature	There is good evidence that lowering the embryo culture temperature to 36°C from 37°C does not improve the embryo implantation rates.
	Dynamic vs. static embryo culture	There is good evidence that dynamic embryo culture does not yield better blastocyst or implantation rates when compared with static embryo culture.
	Number of vitrification cycles	There is fair evidence that double vitrification and double biopsy of a blastocyst can negatively impact the implantation potential of euploid blastocysts.

Embryo factor

- Morphology
- Expansion stage
- Timing of blastocyst formation
- Mitochondrial DNA level

Uterine factor

- Endometrial appearance
- Endometritis
- Previous Obstetrics history
- Adenomyosis and endometriosis
- Arcuate uterus
- Endometrial disruption

Patient factor

- Maternal age
- Paternal age
- Sperm DNA fragmentation
- Body mass Index
- Vitamin D level
- TSH level
- MTHFR

IVF Protocol

- Ovarian stimulation
- Type of trigger
- FET protocol
- Fresh vs frozen ET
- Time of transfer
- P4 level

Embryo Protocol

- Timing/ size of biopsy
- Type of culture media
- Culture temperature
- Number of vitrification cycle

Embryo factor

- Morphology
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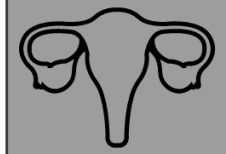

Uterine factor

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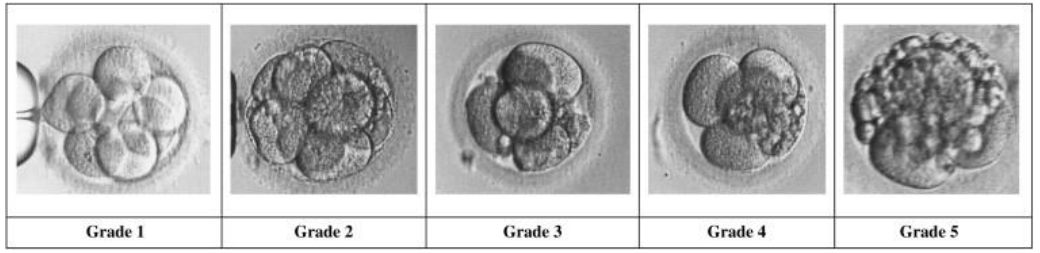
Embryo factor

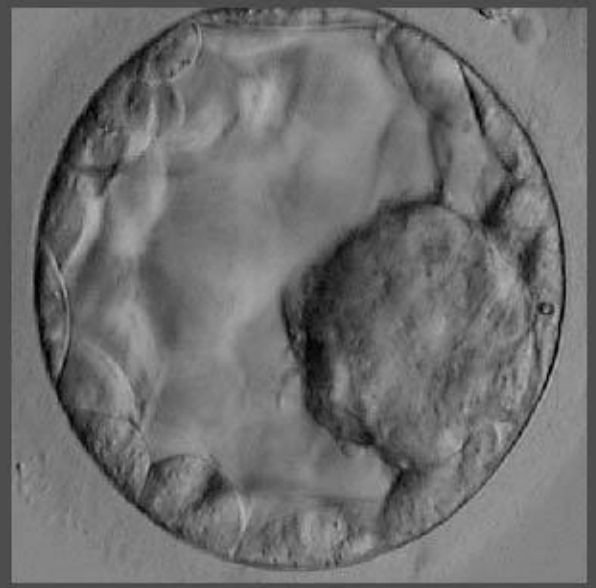
Morphology



- Blastocyst grading/morphology is a widely used marker to assess embryo quality
- Morphology alone is not accurate enough to reliably exclude aneuploidy embryo
- **Excellent embryos resulted in better ongoing pregnancies**
- **Grading of the blastocyst inner cell mass (ICM) grade** was the **most reliable** predictor of pregnancy outcomes
  - Grade A ICM had better live birth rate than Grade C ICM(55.6% vs. 32.3%, P< 0.001)

Morphological grading should be used to **guide selection among euploid embryos**

Original



Embryo Grade:

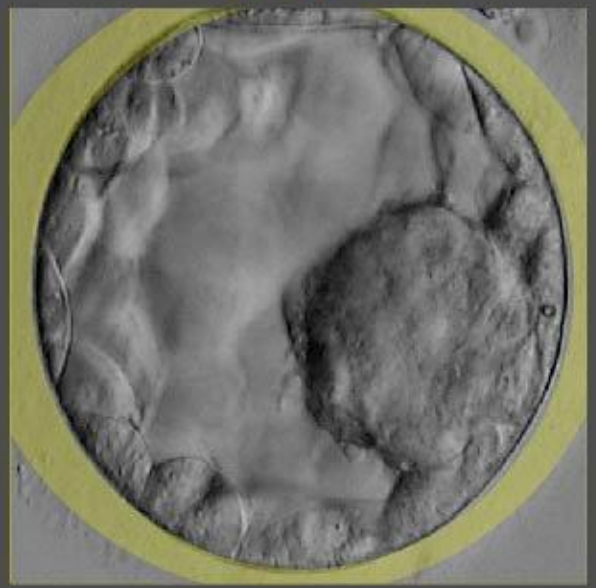
Expansion
"3" based on zona thinness

3AA

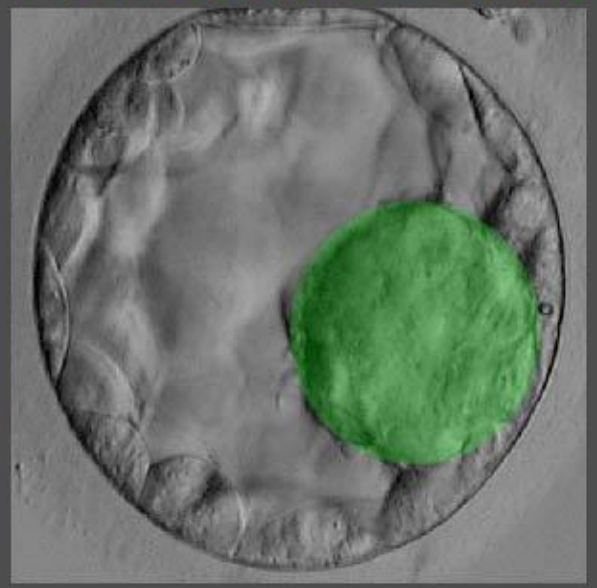
Trophectoderm
lots of cells, "scalloping" of cells around the edge = "A"

Inner cell mass (ICM)
lots of cells, packed = "A"

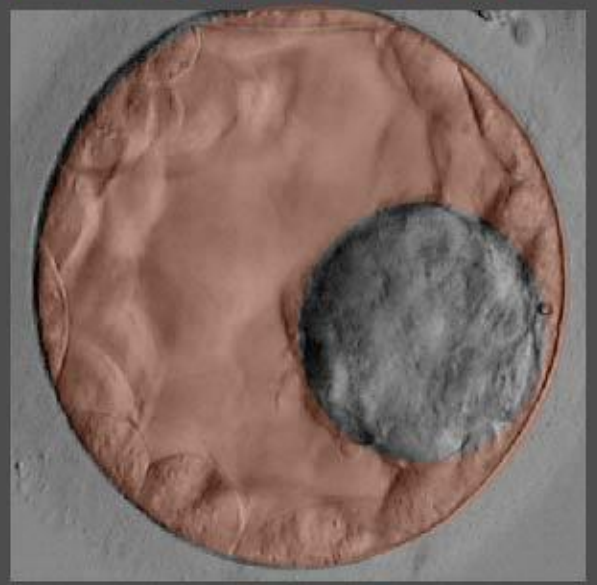
Zona

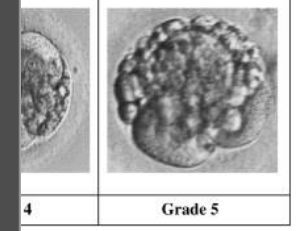


Inner cell mass (ICM)



Trophectoderm

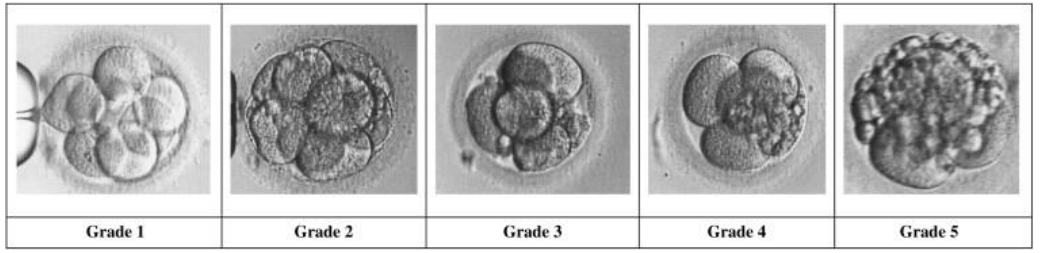




4 Grade 5

Embryo factor

Morphology



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Embryo factor

Expansion stage

- Extended culture media and PGT-A result in the transfer of a more developed and often fully hatched embryo
- A fully hatched embryo may be more vulnerable to trauma during biopsy, cryopreservation, warming, and transfer

Fully hatched vs. nonfully hatched embryo

- Fully hatched embryos had **a trend toward poorer results** of **being retained in the transfer catheter**, **survival rate after warming**, and **implantation rates**, **biochemical pregnancy**, and **early pregnancy loss rates** (similar)
- **A significantly higher likelihood of ongoing pregnancy** or **live birth** in blastocysts within the zona pellucida

Euploid embryo with an intact zona pellucida should be prioritized

Embryo

Expansion stage

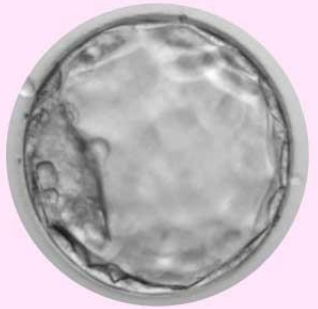
1

Early blastocyst

2

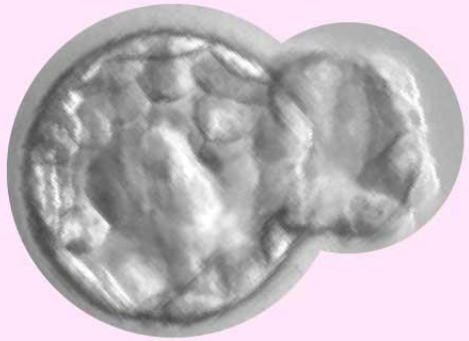
Late blastocyst

3



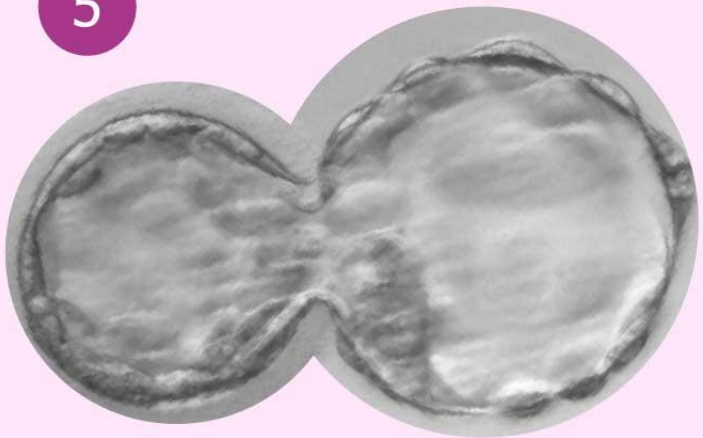
Expanded blastocyst

4



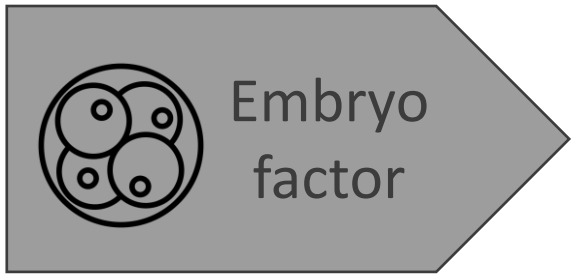
Initiating hatching process

5



During hatching

Euploid embryo with an intact zona pellucida should be prioritized



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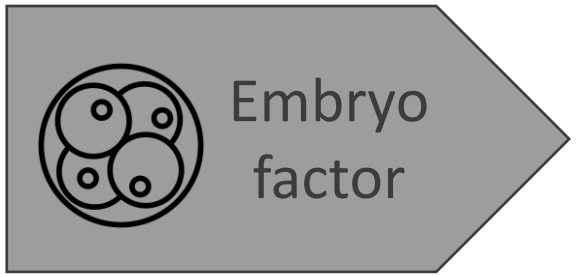


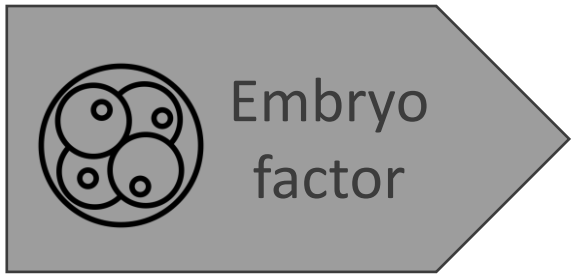
Timing of Blastocyst formation

- Culture through day 7 in some centers increases the pool of transferable embryos
- **Day 7 blastocysts** have a **higher likelihood of aneuploidy** than day 5 and 6 blastocysts.

Day 7 vs. Day 5, 6 blastocyst

- NGS-tested euploid **day 7 blastocysts**, the **pregnancy rates** were slightly **reduced** (no significance)
- **A significant reduction in the euploidy** for **day 7 blastocysts** compared with those for day 5 and 6 blastocysts (40.5% vs. 54.7%, 52.9%)
- **Day 7 euploid blastocyst had a significant decrease** in the **implantation, clinical pregnancy, and live birth rates**

Selection of **day 5 and 6 blastocysts** over day 7 blastocysts



Mitochondrial DNA level

- Mitochondrial function and adequate energy production in the early stages of development are crucial to successful implantation and pregnancy

Previous vs. Current study

- Previous: the **higher amounts of mtDNA** in euploid embryos are linked **to decreased implantation potential**
- Current**: no difference** in mtDNA from delivered vs. nondelivered embryos

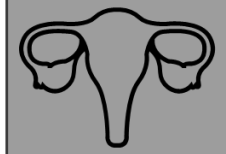
Threshold of mtDNA (unsuccessful implantation)

- **Ongoing pregnancy rate** for embryos with **unusually high mtDNA** levels was **0**

Further study is still needed if mtDNA assessment was clinically useful

Embryo factor

- Morphology
- Expansion stage
- Timing of blastocyst formation
- Mitochondrial DNA level



Uterine factor

- Endometrial appearance
- Endometritis
- Previous Obstetrics history
- Adenomyosis and endometriosis
- Arcuate uterus
- Endometrial disruption

Patient factor

- Maternal age
- Paternal age
- Sperm DNA fragmentation
- Body mass Index
- Vitamin D level
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IVF Protocol

- Ovarian stimulation
- Type of trigger
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- P4 level
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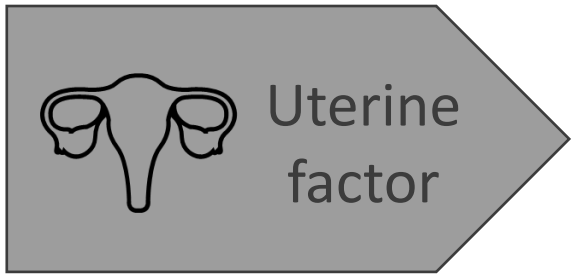
Embryo Protocol

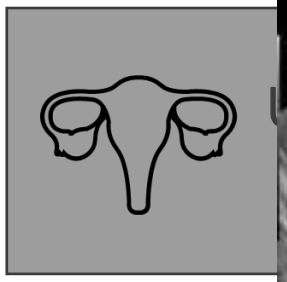
- Timing/ size of biopsy
- Type of culture media
- Culture temperature
- Number of vitrification cycle



Endometrial appearance

- Endometrial appearance, specifically **thickness** and **pattern**, has been proposed as a marker for IVF success (Pelvic ultrasound is the most accessible and least invasive means)

- **Endometrial thickness** **(<8 or >8 mm)** , had **no effect** on the **implantation, pregnancy, or clinical pregnancy rates** (at trigger or transfer day, both fresh and frozen cycles)
- **Mid-late secretory endometrial pattern** had **lower implantation rates**, significantly **higher progesterone (P4) levels** at time of trigger
  - Increased P4 level causes the asynchrony between the embryo and endometrium that leads to decreased implantation rates in fresh ETs



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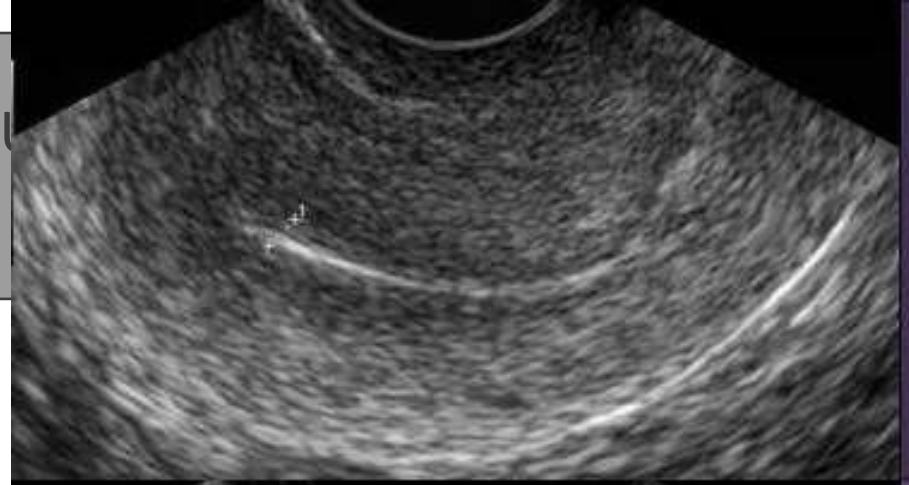
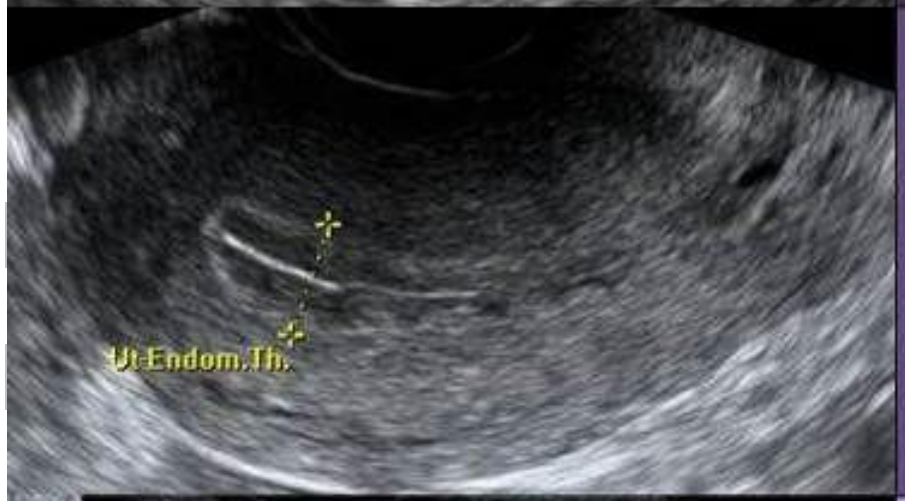
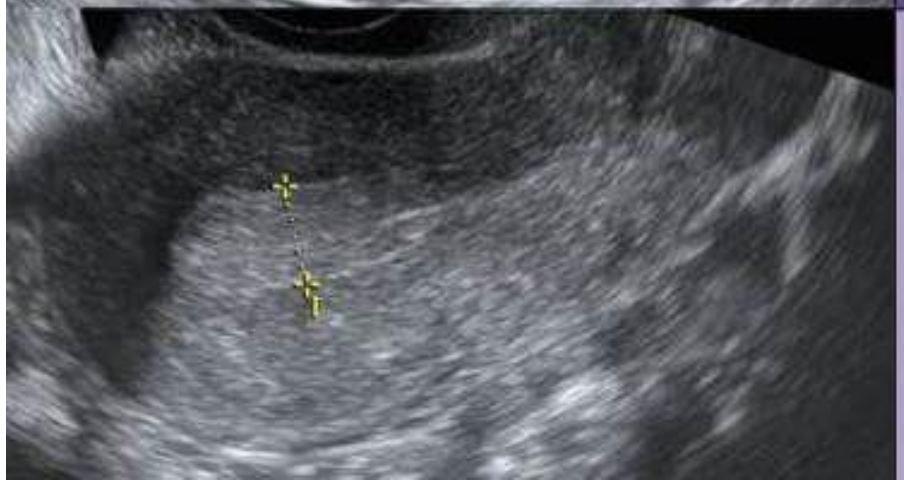
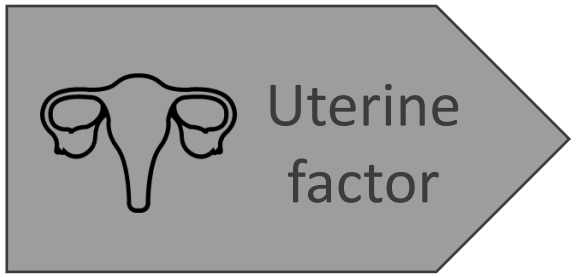
	Early proliferative phase endometrium	•Thin •Linear •Echogenic
	Late proliferative phase endometrium	•Thick •Trilaminar appearance: 1. Central thin, echogenic line 2. Darker echolucent rim in the middle 3. Surrounding echogenic basilar layer
	Secretory phase endometrium	•Thick •Hyperechoic •Homogeneous



Endometrial appearance

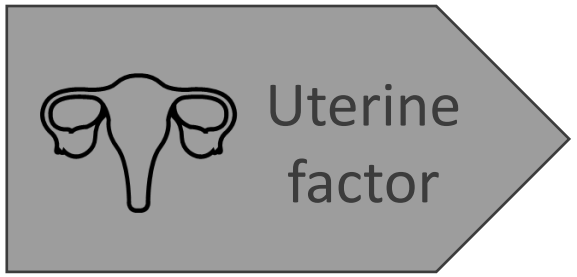
Endometrial compaction

- The absolute change in endometrial thickness between the end of the proliferative phase and the day of transfer
- May be a marker for reproductive success

Previous vs. Current study

- **Higher ongoing pregnancy rates** compared with cycles without compaction
- **Endometrial compaction of >10%** (measured by transvaginal ultrasound) lead to **higher clinical pregnancy rates** in frozen euploid ETs
- Current: **no increase** in the **clinical pregnancy or live birth rates** with EM compaction (>5% decrease in endometrial thickness)
  - Discrepancy: TVS before ET day vs. TAS at ET day

Influence of **EM compaction** on IVF outcomes remains **unclear**

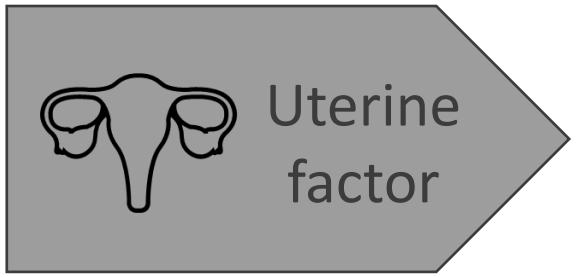


Endometritis

Chronic endometritis (inflammation of the endometrium)

- Generally asymptomatic
- Associated with poor reproductive outcomes
- Immunohistochemical staining for the cell marker CD138 (plasma cell in EM stroma)

- Approximately **one third of** women with recurrent implantation failure are diagnosed with chronic endometritis
- **Recurrent implantation failure** successfully treated for chronic endometritis have **improved implantation, clinical pregnancy, and live birth rates** similar to those **without endometritis**



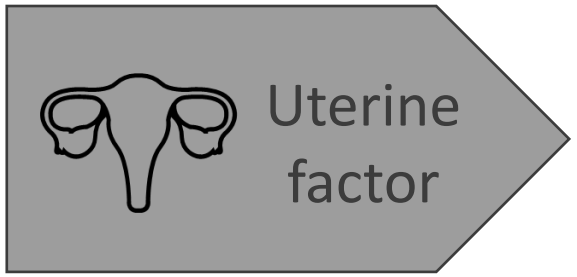
Previous Cesarean Delivery

- Patient with previous history of cesarean delivery had decreased implantation and live birth rates

Previous cesarean vs. vaginal delivery

- **Lower implantation rates** in **previous cesarean delivery** patient
- A statistically significant difference in the **implantation and ongoing pregnancy rates** (68.0% vs. 55.5% (P= 0.004)), **live birth rates** (59.1% vs. 49.0% (P=0.02)) between previous vaginal vs. cesarean delivery

Cesarean delivery should **be limited** to reduce down-stream effects on fertility



Adenomyosis and Endometriosis

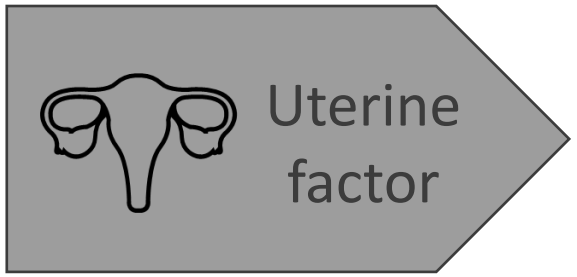
- **Adenomyosis** has been implicated in **poor IVF outcomes** (lower implantation, clinical pregnancy, and live birth rates, along with higher miscarriage rates)

3D-TVS before ET day (648 euploid embryo)

- The **clinical pregnancy, miscarriage, and live birth rates** were **similar** between adenomyosis and control group when controlling for confounders, including age at transfer and BMI
- Asymptomatic adenomyosis had a lesser effect on reproductive outcomes

Retrospective study (euploid embryo and successful conceived)

- **Higher miscarriage rates** in women with adenomyosis (biochemical miscarriage)
- **Lower beta-hCG values** at 16 days after ovulation

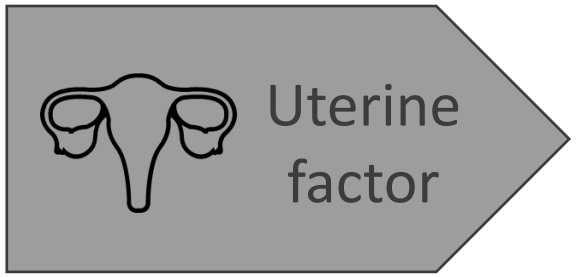


Adenomyosis and Endometriosis

- **Routine screening** for adenomyosis before ET is **not currently indicated**
- Some have recommended interventions such as **gonadotropin-releasing hormone (GnRH) suppression** before transfer

Endometriosis

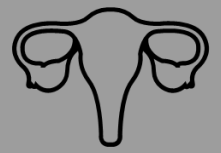
- Result in worse laboratory and clinical outcomes
  1. Impaired endometrial receptivity
  2. Oxidative stress and increased free radicals may result in impaired embryo development
- Compared with male factor infertility
  1. No statistically significant difference in **live birth rates**
  2. **Aneuploidy rates** was similar



Arcuate Uterus

- Convex fundal contour with shallow endometrial indentation
- The most common congenital uterine anomaly in the general population and women with recurrent pregnancy loss
- There was **no difference** in the **implantation** (63.7% vs. 65.4%), **live birth** (68.7% vs. 68.7%), **chemical pregnancy** (8.4% vs. 7.7%), or **miscarriage** (4.8% vs. 4.3%) rates between **women with an arcuate** and those with normal uterus.

Surgical intervention for arcuate uterus is **not necessary** before euploid ET



Uterine factor

Endometrial Disruption

- Known as endometrial scratch, an effective intervention for women with implantation failure
- Recruitment of cytokines, growth factors, and other inflammatory molecules to the endometrium

Endometrial scratching(n=690) vs. no intervention(674)

- **No difference** in the **live birth rates, clinical pregnancy, ongoing pregnancy, or miscarriage rates**

High risk group with prior euploid ET failure

- The **clinical implantation** and **sustained implantation rates** were **equivalent**

Endometrial disruption does **not** appear to have a beneficial effect

Embryo factor

- Morphology
- Expansion stage
- Timing of blastocyst formation
- Mitochondrial DNA level

Uterine factor

- Endometrial appearance
- Endometritis
- Previous Obstetrics history
- Adenomyosis and endometriosis
- Arcuate uterus
- Ease of transfer
- Endometrial disruption

Patient factor

- Maternal age
- Paternal age
- Sperm DNA fragmentation
- Body mass Index
- Vitamin D level
- TSH level

IVF Protocol

- Ovarian stimulation
- Type of trigger
- FET protocol
- Fresh vs frozen ET
- Time of transfer
- P4 level
- Previous vitrified egg

Embryo Protocol

- Timing/ size of biopsy
- Type of culture media
- Culture temperature
- Number of vitrification cycle

Maternal Age

- Increasing maternal age is the most significant factor contributing to the inability of generating chromosomally competent embryos

Prior vs Current Study

- **Selective transfer of a euploid embryo** demonstrated equivalent implantation and pregnancy rates
- Current: The implantation rates were **negatively correlated with age**
  - **OR compared with the youngest group** (women aged <35 years) of 0.85 (age 38–40), 0.69 (age 41–42), and 0.51 (age >42)
- **Very advanced age** likely remains an important factor in euploid embryo success

Paternal Age

- It is possible that sperm from older men could produce embryos with lower reproductive potential

Systemic review of 7 studies

- Most of them found **no statistically significant** relationship between **paternal age** and **achieving pregnancy, liver birth rate**

IVF outcome with only euploid embryo

- **Fertilization rates** were **negatively** impacted with **increasing paternal age**
- **Implantation and pregnancy rates** were **not** significantly different when maternal age was controlled

Sperm DNA fragmentation

- Advanced paternal age has also been linked with increased sperm DNA fragmentation (SDF)
- SDF is a new diagnostic tool for evaluating semen quality in men with infertility

Low DFI (<15%) vs. High DFI(>15%)

- Assessed the direct impact of SDF on IVF outcomes, control embryonic euploidy
- **High DFI group** were **older** and had **lower total motile sperm** and **lower sperm concentration** than low DFI group
- **No** clinically significant differences in the **implantation or ongoing pregnancy rate** in either group

SDF on the day of fertilization may not impact the euploidy rates or pregnancy outcomes

Body Mass Index

- BMI appears to have the most significant impact on the euploid ET success rates
- Obesity is a known risk factor for increased miscarriage rates

Lean(BMI: 18.5-24.9) vs. Overweight(25-29.9) vs. Obese(>30)

- **Lean patients** had significantly **lower miscarriage rates** than overweight and obese patients (14%, 29%, and 42%)

Retrospective study in 2020

- Patients who achieved a live birth had a **significantly lower BMI** than patients who did not (22 vs. 27 kg/m2)

Vitamin D level

- Prior study: vitamin D deficiency with preeclampsia and small-for-gestational-age infants

Vitamin D deficient (<20 ng/mL) vs. insufficient (20–29.9), replete (>30)

- No differences in the implantation, clinical pregnancy, or ongoing pregnancy rates after a euploid ET in either group

Low vitamin D levels likely have **no impact** on pregnancy outcomes

TSH level

- **Current recommendation:** maintain a TSH level of <2.5 mIU/L in women attempting conception and during early pregnancy

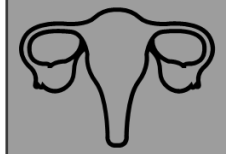
TSH measured 8 days after ET

- Analyze **optimal range of TSH below 2.5 mIU/L** that impact the IVF success rates with euploid embryos
- **No** differences were observed in the **implantation, live birth, or miscarriage rates** by the TSH levels.
- **No** difference in the live birth rates for those on **levothyroxine vs. no supplement**

Variations of TSH levels < 2.5 mIU/L do **not** seem to have an effect on pregnancy outcomes

Embryo factor

- Morphology
- Expansion stage
- Timing of blastocyst formation
- Mitochondrial DNA level



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Ovarian Stimulation

- Optimize the number of oocytes retrieved while minimizing the risk of ovarian hyperstimulation.

Stimulation length/gonadotropin dose vs. euploidy or live birth rate

- Higher doses of gonadotropins, more prolonged ovarian stimulation, higher estradiol levels, follicular size at time of trigger, and higher number of oocytes retrieved **did not have a negative impact** on the **euploidy** or **live birth rates**

No toxic effect of gonadotropin administration on **aneuploidy risk** or **euploid embryo reproductive potential**

Type of Trigger

- Final oocyte maturation before oocyte retrieval can be achieved by the administration of hCG or GnRH agonist (alone or in combination)
- **The hCG trigger** is known to increase the risk of OHSS in high responders due to its **long half-life of 24 hours** or more (GnRH: 60min)

GnRH agonist vs. hcG trigger

- No statistically significant difference in the ongoing pregnancy and live birth rates using either a GnRH agonist (n=145) or an hCG trigger (n=118)

No evidence the **type of trigger for final maturation** before oocyte retrieval affects the implantation potential of euploid embryos.

FET Protocol

- The successful implantation of an embryo depends on the transfer of a viable embryo into a receptive endometrium
- **Natural cycle (NC), modified natural cycle:** avoidance of multiple medications
- **Artificial cycle (AC):** better control over ET timing and avoidance of premature ovulation

Modified-NC vs. AC

- **No significant differences** in the clinical pregnancy, implantation, or miscarriage rates

NC vs. AC (anovulatory patient)

- **NC** single frozen euploid ET was associated with **significantly higher ongoing pregnancy rates**
- **The duration of estrogen administration** before frozen euploid ET **did not** impact the **implantation, clinical pregnancy, or live birth rates**

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More data are needed on the outcomes of FET using an NC vs. AC

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Timing of Transfer

- The implantation and live birth rates after the first euploid ET are close to 70% and 65%
- One of the other factors described as a source of implantation failure is **endometrial receptivity**
- **The endometrial receptivity assay (ERA):** detect displaced window of implantation (WOI) after history of implantation failure

Personalized FET vs without personalized

Not statistically significant based on the small sample size

- 22.5% were found to have a displaced WOI with at least 1 failed euploid FET
- **pFET** had **higher implantation and ongoing pregnancy rates** than without personalized FET
- **Nonsignificant lower implantation rate** after **personalized euploid FET** cycles

No data to suggest the **timing of the transfer** can be altered to increase successful implantation or clinical pregnancy.

P4 level

- **P4 produced by the corpus luteum** is required for successful embryo implantation and pregnancy maintenance until the luteal placental shift
- **Progesterone supplementation** during the **luteal phase of frozen ET cycles** increase live birth rates
- Unfavorable outcomes when a **premature increase in the P4 level** is detected after ETs in fresh IVF cycles

P4 levels on day 19 of euploid FET

- P4 levels **between 10 and 20 ng/mL** on day 19 were optimal
- The ongoing pregnancy and live birth rates **decreased** when the **P4 level was >20 ng/mL**
- Elevated P4 levels (on Day 19) may **shift the WOI** that decreased success rates
- **No consensus** on the most **optimal P4 level** on the ET day (affected by range of P4)

P4 level

P4 level on trigger day

- **Number of eggs retrieved** and the **number of euploid embryos available** for future ET were not affected by the P4 levels
- **Elevated P4 levels of >1.5 ng/mL** on the day of trigger did not affect the pregnancy and live birth rates in the first subsequent frozen euploid ET

Fresh vs. Frozen ET

Fresh ET

- More immediate transfer, limit the costs and risks of vitrification/warming and storage of embryos
- Patients don’t have to wait weeks to months to attempt transfer (less stressful)
- Requires expanded blastocysts on day 5 and at least 1 euploid embryo for ET

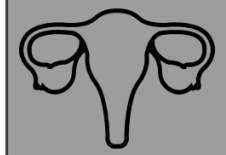
Frozen ET

- Depends on the high survival rate of embryos during the vitrification/warming process
- **Higher ongoing pregnancy rates, live birth rates, lower preterm delivery and low birth weight**

Better outcomes with the **freeze-all option** with euploid embryos transfer

Embryo factor

- Morphology
- Expansion stage
- Timing of blastocyst formation
- Mitochondrial DNA level



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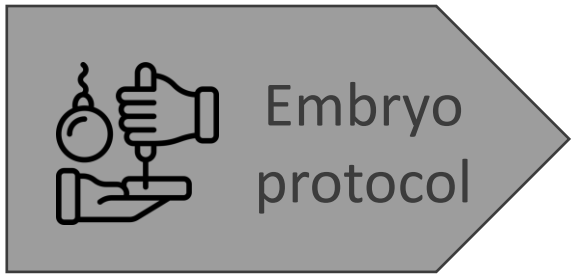


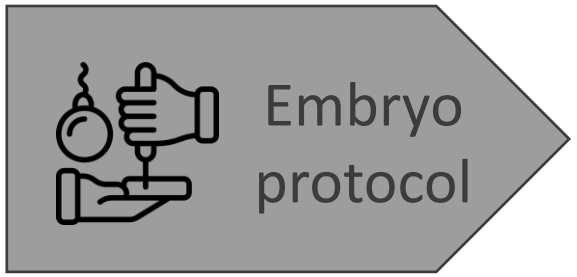
Timing of Embryo Biopsy

- PGT has been used extensively to assist in the selection of the best embryo

Blastomere biopsy of cleavage-stage embryos vs. trophectoderm biopsy of blastocysts

- **Cleavage-stage biopsies** can provide adequate DNA samples but can also be harmful to the embryo
- Only **30% of cleavage-stage** biopsied embryos sustained implantation and led to live-born infants (unbiopsied controls: 50%)
- Embryos biopsied at **the blastocyst stage** had equivalent implantation rates (51% vs. 54%) as unbiopsied controls
- Significantly reduced ongoing pregnancy rates in women assigned to **cleavage- stage biopsy**

Reduced viability and implantation rates with **cleavage-stage** embryo biopsies

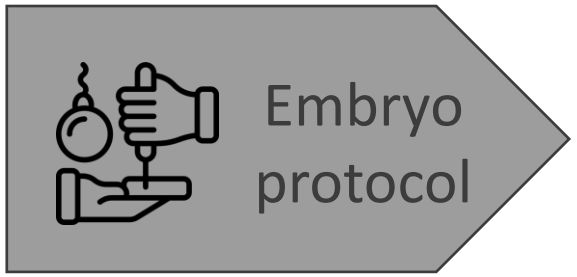


Size of trophectoderm biopsy

- Size of the biopsy during PGT-A has an impact on the euploid embryo implantation rates
- **Cleavage-stage biopsy:** removal of 1 or 2 cells from an embryo containing only 6–10 cells
- **Blastocyst biopsy:** removal of 5–10 trophectoderm cells from hundreds of cell

Trophectoderm biopsy size vs. pregnancy outcome

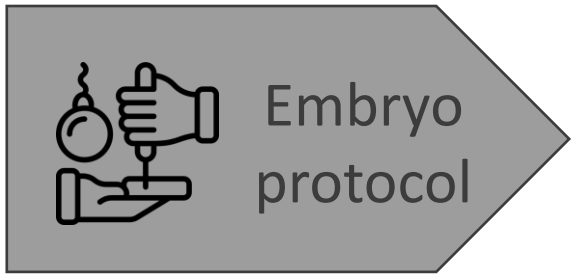
- Trophectoderm biopsies with the **relatively highest DNA content** were correlated with a lower chance of implantation and ongoing pregnancy
- Determine the exact number of biopsied cells is difficult, and smaller biopsy could lead to uninterpretable results



Type of culture media

- **Monophasic media:** use only 1 type of culture to support the growth and development of the embryo to the blastocyst stage
- **Sequential media:** changing the constituents of the media after the third day of development
  - Mimic the changing metabolic and physiologic processes of the growing embryo

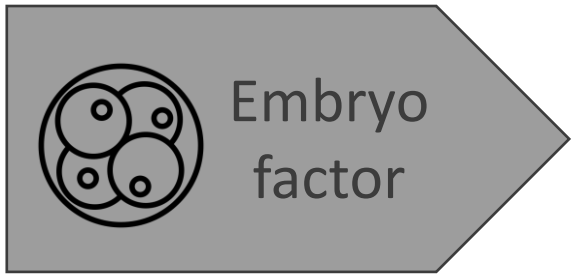
- A significantly higher blastulation rate was observed with **sequential media** (55% vs. 47%)
- The euploidy rate, implantation rates were **equivalent** between the 2 groups

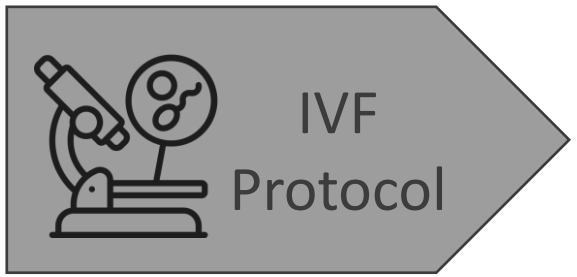


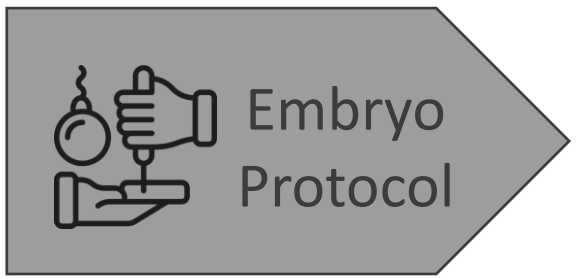
Number of vitrification cycle

- **Comparable clinical pregnancy rates** in embryos that underwent **double vitrification with a single biopsy** (44%) vs. **single vitrification and single biopsy** (46%)
- A trend toward **lower clinical pregnancy rates** in the **double vitrification and double biopsy** group (35%), which was not statistically significant

- **Double vitrified and double biopsied embryos** had a significantly **reduced clinical pregnancy rate** (vs. single vitrified and single biopsy)





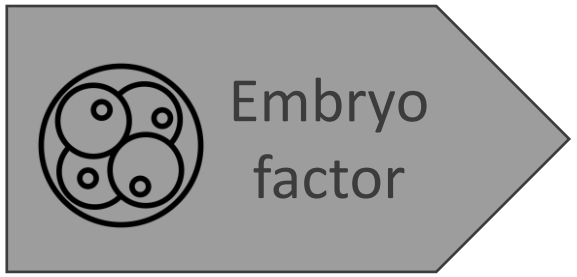


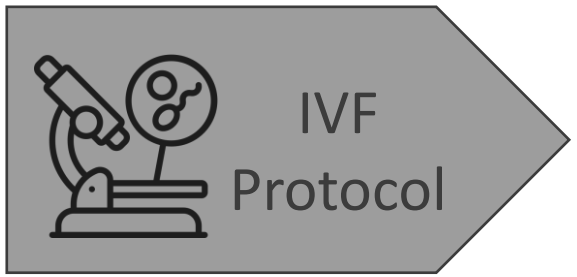
V ➢ Morphology — Better morphological grade, better ICM grade

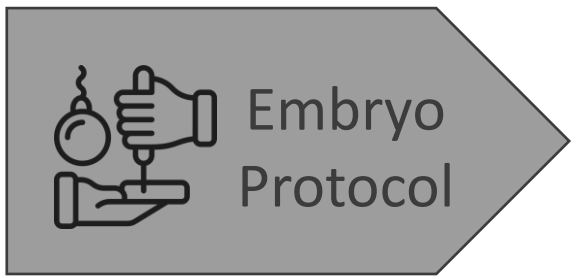
V ➢ Expansion stage — Embryo with an **intact zona pellucida**

V ➢ Timing of blastocyst formation — Selection of **day 5 and 6 blastocysts** over day 7

X ➢ Mitochondrial DNA level







V • Endometrial appearance

V • Endometritis

V • Previous Obstetrics history

V • Adenomyosis and endometriosis

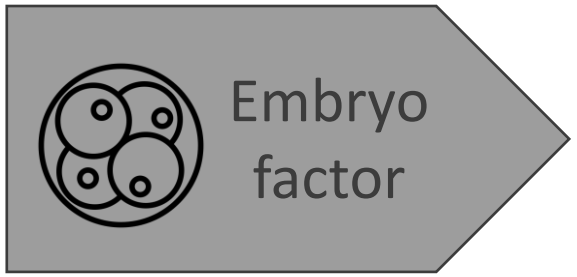
X • Arcuate uterus

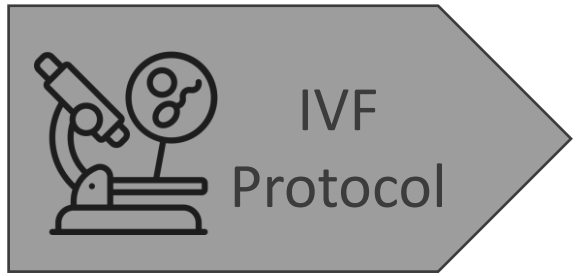
X • Endometrial disruption

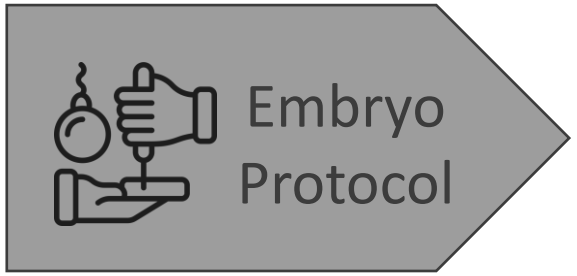
P4 level before ET more predictive of implantation success than appearance and thickness

Improved reproductive outcomes after **treatment**

Associated with a **higher risk of euploid loss**







V ➢ Maternal age

X ➢ Paternal age

X ➢ Sperm DNA fragmentation

V ➢ Body mass Index

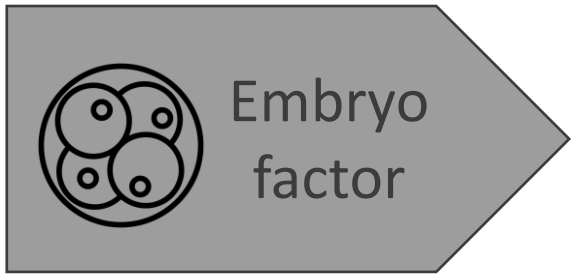
X ➢ Vitamin D level

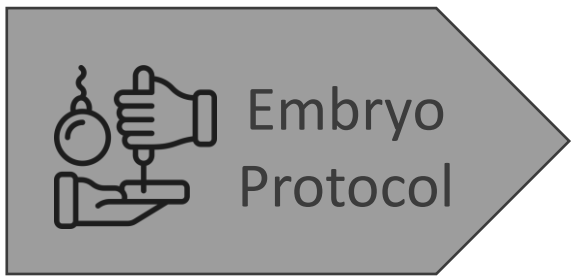
V ➢ TSH level

Reduced implantation over the age of 40 years

Overweight and obese patients are more like to experience a spontaneous abortion

Higher levels may be linked with spontaneous abortion





V • Ovarian stimulation

X • Type of trigger

X • FET protocol

V • Fresh vs frozen ET

X • Time of transfer

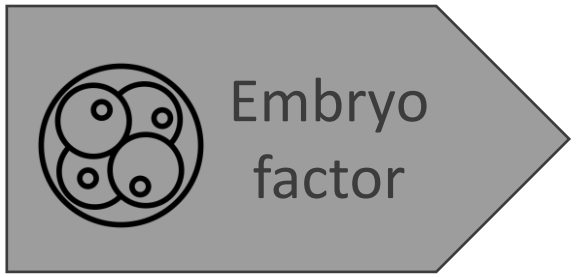
V • P4 level

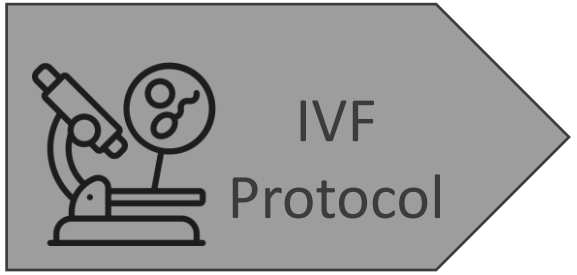
Aggressive ovarian stimulation protocols may increase the number of euploid embryos obtained

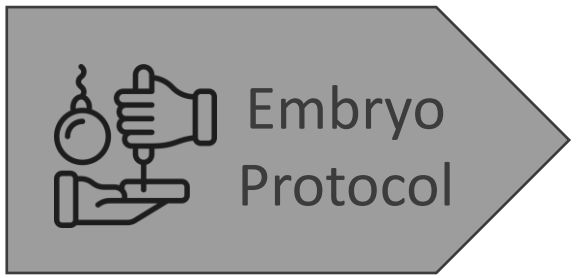
Frozen transfer potentially improve outcomes in selected patient populations

No consensus on the optimal P4 level

Elevated levels above a minimum threshold are harmful







V ➢ Timing/ size of biopsy

X ➢ Type of culture media

V ➢ Number of Vitrification Cycles

Trophectoderm biopsy being superior to cleavage-stage biopsy

Double vitrification/double biopsy negatively impact pregnancy rate

Thank you for listening!!

Speaker：R3 張嘉文
Supervisor: 黃貞瑜 醫師