Royal Hospital for Women (RHW)
BUSINESS RULE
COVER SHEET

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SUMMARY	This clinical business rule has been developed to guide clinical practice of an embryo transfer cycle at the Fertility & Research Centre, Royal Hospital for Women. It assists in determining the appropriate management including treatment types, monitoring, and prevention management of adverse outcomes.
KEYWORDS	Frozen Embryo Transfer (FET), Artemis (fertility based reportable database), Follicle Stimulating Hormone (FSH), Luteal Phase Support (LPS), Assisted Reproductive Technology (ART).

Royal Hospital for Women (RHW)
BUSINESS RULE

Health
South Eastern Sydney
Local Health District

In Vitro Fertilisation (IVF) - Embryo Transfer — RHW CLIN102

Contents

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Within this document we will use the term woman, this is not to exclude those who give birth and do not identify as female. It is crucial to use the preferred language and terminology as described and guided by each individual person when providing care.

1 BACKGROUND

The aim of this CBR is to provide support and guidance for the management of an embryo transfer cycle. An embryo transfer is defined as a fertilised oocyte that is transferred into the uterus to try to establish a pregnancy, there are two types of embryo transfers offered.

- Embryo transfer (ET) – where the fertilised oocyte is transferred into the woman's uterus 3-5 days after an egg collection, within the same cycle, also referred to as fresh embryo transfer.
- Frozen embryo transfer (FET) – a previously created embryo, (that has been cryopreserved) is thawed on the day of transfer and transferred into the woman's uterus.

2 RESPONSIBILITIES

2.1 Medical Director

Oversee all policy development and supports clinical practice of fellows/registrars

2.2 Medical staff – Management of embryo transfer cycles inclusive of individualised care, monitoring of results, consenting to treatment, counselling and clinical practice

2.3 Embryology Staff – Appropriate handling of embryos, documentation, collaborative care within multidisciplinary team

2.4 Registered Nurses - Coordination, education and support to patients undertaking embryo transfer cycles inclusive of direct patient contact, counselling and monitoring.

3 PROCEDURE

3.1 General Principles

The decision to transfer an embryo is at the discretion of the overseeing medical officer, as is the choice of protocol used in the management of the cycle. As a rule, only one embryo is to be transferred at a time to reduce the risk of maternal and fetal adverse outcomes. If a patient requests more than one embryo to be transferred, it is up to the clinician to determine the safety based on the patient's individual history and in discussion with the woman.

3.2 Clinical Practice

3.2.1 Fresh Embryo transfer

Fresh embryo transfers occur 5 days after oocyte collection with day 1 being the day following oocyte collection (with the exception of Monday oocyte collections, whereby a fresh embryo transfer may occur 4 days post oocyte collection). Education for patients surrounding embryo transfer should be provided at nursing orientation prior to commencing an In Virto Fertilisation (IVF) superovulation cycle.

Preparation

- Confirm plan for transfer with medical team
- *Refer to In Vitro Fertilisation (IVF) - Management and Treatment of a Superovulation Cycle*
- Ensure patient has administered a Recombinant human chorionic gonadotropin (r-hCG) trigger of choriogonadotropin alfa (Ovidrel®) 36 hours prior to oocyte collection
- Advise patient on day of Oocyte Pick-Up (OPU) trigger instructions to commence luteal phase support Luteal Phase Support (LPS) day 1 post egg collection
- Contact patient for luteal call day 1 post egg collection confirm plan to commence LPS based on confirmation from embryology lab of oocyte fertilisation If nil oocyte fertilisation escalates to medical team to arrange plan for patient
- Coordinate with medical team and embryology lab to arrange time for fresh embryo transfer on day 4 or 5 post oocyte collection based on day of OPU as explained above.

Day 3 embryo transfer

- Where poor embryo development has been identified by the embryology lab or a history of embryo arrest on day 3 the supervising clinician may advise of a day 3 transfer. Patients are to be given instructions as per day 5 transfer

3.2.2 Frozen Embryo transfer

Starting the cycle

- Patients are to contact the RHW Fertility & Research Centre (FRC) nursing team to notify day 1 of full flow menstruation.
- Confirm embryo transfer treatment plan with patient
  - If not documented, discuss with medical team
  - Ensure patient has an embryo suitable for transfer

Inducing a period to start a cycle

Anovulatory patients may be advised to commence Medroxyprogesterone (Provera®) 10mg daily for 7-10 days OR Levonorgestrel + Ethinylestradiol (Microgynon®) 30 ED 1 x tablet daily for 10-12 days to induce a period to commencing an embryo transfer cycle

Natural Cycle

- Document last menstrual period (LMP) start date of cycle
- Arrange blood test (Oestradiol, Luteinising Hormone, Progesterone) appointment on day 9 of cycle unless menstrual cycle length is < 28 days (use clinical judgement to book in earlier appointment based on cycle length)
- Monitor patients cycle via blood tests and ultrasounds every 1-4 days as determined by the medical team
- Observe for LH surge, which typically occurs 36 hours prior to ovulation

  - LH surge is defined as >25 IU/L **OR** double the baseline LH level in patients with Polycystic ovary syndrome (PCOS)
- Observe for uterine endometrium >7mm (if <7mm medical team may still proceed based on clinical judgement) and presence of a dominant follicle
- Ovulation should occur the day following LH surge and be indicated by a rise in progesterone level >5 nmol/L
- Monitor serum hormone levels if ovulation is not clear, every 1-2 days at the discretion of the medical team until ovulation is clear and determined by medical team
- Book embryo transfer based on LH surge + 5 days
- Advise patient to commence LPS day 1 post ovulation or 2 days post LH surge, as prescribed see **Appendix A & B**

Modified natural cycle

Involves monitoring of a natural menstrual cycle (as above) and includes the use of 250mcg of Choriogonadotropin alfa(hCG) (Ovidrel®) to assist ovulation and assist timing a transfer when:

  - Follicle measures >16mm mean diameter
  - Uterine endometrium is >7mm (if <7mm medical team may still proceed based on clinical judgement)
  - Estrogen levels >500pmol/L and Progesterone level <3nmol/L

- Book patients in for blood test and ultrasound on Day 9 of cycle, if Day 9 falls on a Saturday or Sunday patient to be seen on the Friday prior
- Aim for patient to self-administer hCG trigger on a Friday **OR** Monday if patient meets criteria as above

When a hCG trigger is used, predicted ovulation occurs around 40hrs and therefore embryo transfers should be scheduled at approximately168 hours (7 days) after the hCG trigger is administered.
Refer to **Appendix A & C** for LPS instructions.

Ovulation induction using Follicle Stimulating Hormone (FSH)

- Advise patient to commence FSH on day 4 of their cycle, to continue FSH daily at the same time as decided by the patient
- Book initial blood test and ultrasound on day 9 of their cycle, if day 9 falls on a Saturday or Sunday, patient to be booked on Friday prior
- Monitor patients cycle via blood tests and ultrasounds every 1-4 days as determined by the medical team
- Medical team to determine timing of r-hCG trigger based on parameters discussed under ‘natural’ and ‘modified natural cycle’
- Advise patient to cease use of FSH on day of hCG trigger
- Refer to **Appendix A & C** for LPS instructions

Ovulation induction using Letrozole

- Advise patient to commence Letrozole at prescribed dose on day 2 of their cycle, final dose to be administered on day 6 of their cycle

- Manage the cycle as specified under Ovulation induction using Follicle Stimulating Hormone (FSH) and trigger as per Modified natural cycle

Hormone replacement therapy (HRT)

HRT cycles are utilised at the discretion of the medical team and not routinely used as first line management for frozen embryo transfer cycles. The managing doctor may prescribe HRT on an individual basis based on history of poor response, to facilitate specific timing of a transfer, or in patients who have undergone a premature menopause.
Estradiol valerate is dispensed in 2mg tablets with prescribed daily dosages between 4-8mg.

- Advise patient to commence Estradiol on day 2 of their cycle as prescribed e.g 2mg TDS = 6mg/daily
- Ensure patient continues Estradiol valerate at the same times every day
- Book a blood test and ultrasound scan appointment day 10-14 of cycle
- Continue to monitor via blood test and ultrasound scan appointments (at the discretion of the medical team)
    - Serum progesterone levels should remain <3nmol/L
    - Ovaries should remain unstimulated
- Plan embryo transfer when endometrium is deemed suitable for transfer by medical team
- Instruct the patient to commence progesterone pessaries, patients should have 120 hours of progesterone prior to embryo transfer. Refer to **Appendix A & D**

Day of embryo transfer

Prior to embryo transfer ensure the woman has been contacted and advised of the below embryo transfer instructions;

- Bring photo ID to procedure
- **Avoid wearing fragrances**
- Patient to have full bladder (empty bladder 2 hours prior to procedure and drink water approx. 500mls)
- If utilising progesterone pessaries as LPS advise patient to avoid morning pessary prior to transfer

- Alert attending medical officer and embryology staff of the patient's arrival
- Confirm if patient has made co -payment (if applicable)
- Escort patient to Gynaecology outpatient department on Level 2
- Assist in set -up of embryo transfer room
    - Draw sheet and patient gown available on the bed
    - Ultrasound machine
    - Procedure trolley
    - Speculum
    - Sterile gloves
    - Sterile drape
    - 1 x normal saline ampule (10mls)
    - 1 x cotton tip applicator
    - 1 x embryo transfer catheter (provided by embryology)
- Check consents for procedure have been completed in accordance with level 2 Ministry of Health - Clinical Procedure Safety PD2017_032
- Provide patient with post embryo transfer information sheet

- Ensure patient continues luteal phase support
- Inform patient to attend clinic 10 days post embryo transfer for pregnancy blood test

3.2.3 Pregnancy test results

Positive ß-HCG >100

- Advise patients to continue LPS
- Calculate estimated date of delivery
- Repeat ß-HCG + P4 blood test 7 days post initial blood test result, enter results into Artemis
- Monitor rise in ß-HCG hormone, liase with medical team if abnormal rise in levels
  - As a general rule ß-HCG levels should double every 2-3 days until 6 weeks gestation
  - P4 levels should be >30nmol/L
- Provide patient with ultrasound request form for 1st trimester dating ultrasound and advise to book in at 7 weeks gestation
- Provide patient GP referral letter
- Follow up ultrasound report and enter report findings in Artemis
- Confirm with medical team if patient can cease LPS once dating scan is reviewed
- Contact patient to advise of plan from medical team and ensure pregnancy follow up has been arranged
- HRT cycles: estradiol and progesterone to continue until 12 weeks gestation

Positive ß-HCG <100

- Consult with medical team regarding timing of repeat ß-HCG + P4 blood test
- Minimum 48 hours between initial blood test and repeat ß-HCG + P4
- Consult medical team with each result
- If suspicion of non-progressive pregnancy refer to Early Pregnancy Assessment Service (EPAS).

Negative ß-HCG

- Advise patient to cease LPS
- Offer patient counselling support
- Liaise with medical team regarding next steps for patient
  - Review frozen embryo storage report in Artemis
  - Consider consultant review if ≥3 embryo transfers with negative ß-HCG result

Patients should be advised to use frozen embryos prior to being offered an additional IVF superovulation cycle

3.3 Documentation

- Artemis
- eMR
- Patient fertility file

3.4 Education Notes

- Patient/s seeking embryo transfer must have serology valid within 12 months
- Patient/s must complete relevant consents to treatment
- Fresh embryo transfer (ET) may be clinically indicated where embryos do not appear to be suitable for freeze as directed by the embryology lab

- There is nil significant statistical difference between live birth rates of FET Vs frozen embryo transfers[1]
- Where risk of Ovarian Hyper Stimulation Syndrome (OHSS) is present patients planning for a fresh embryo transfer (ET) will be advised to freeze all embryos
- The FRC must minimise the incidence of multiple pregnancies and therefore a single embryo transfer is advised. On rare occasions the medical team may opt to conduct a double embryo transfer when a valid reason exists.
- Ensure that no more than 2 embryos are transferred in any one treatment cycle in a woman under the age of 40 years at the time of oocyte collection (inclusive of recipient donor cycles)[2]**Error! Bookmark not defined.**
- A single embryo transfer is mandatory for a gestational carrier in a surrogacy arrangement

3.5 Implementation plan

The revised CBR will be distributed to all medical, nursing and midwifery staff via @health email. The CBR will be discussed at ward meetings, education and patient quality and safety meetings. Education will occur through in-services, open forum and local ward implementation strategies to address changes to practice. The staff are asked to respond to an email or sign an audit sheet in their clinical area to acknowledge they have read and understood the revised CBR. The CBR will be uploaded to the CBR tab on the intranet and staff are informed how to access

3.6 Related Policies/procedures

- In Vitro Fertilisation (IVF) - Management and treatment of a Superovulation Cycle
- Intrauterine Platelet Rich Plasma (PRP) Infusion

3.7 References

1. Greenbaum, S., Athavale, A., Hershko Klement, A. & Bentov, Y. Luteal phase support in fresh and frozen embryo transfers (2022) Frontiers Reproductive Health https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9580718/
2. Steinberg Weis, M., Luo, C., Zhang, Y., Chen, Y., Kissen, D., Statten, G & Barnhart, K. Fresh Vs Frozen embryo transfer: new approach to minimize the limitations of using national surveillance data for clinical research (2023) Fertility and Sterility.Vol 119, Issue 2 https://www.sciencedirect.com/science/article/pii/S0015028222019719

4 ABORIGINAL HEALTH IMPACT STATEMENT DOCUMENTATION

Considerations for culturally safe and appropriate care provision have been made in the development of this Business Rule and will be accounted for in its implementation.

When clinical risks are identified for an Aboriginal and/or Torres Strait Islander woman or family, they may require additional supports. This may include Aboriginal health professionals such as Aboriginal liaison officers, health workers or other culturally specific services

5 CULTURAL SUPPORT

For a Culturally and Linguistically Diverse CALD woman, notify the nominated cross-cultural health worker during Monday to Friday business hours. If the woman is from a non-English speaking background, call the interpreter service: NSW Ministry of Health Policy Directive PD2017_044-Interpreters Standard Procedures for Working with Health Care Interpreters.

6. NATIONAL STANDARDS

- Standard1 – Clinical Governance
- Standard 2 – Partnering with Consumers
- Standard 5 – Comprehensive Care
- Standard 6 – Communicating for Safety

7. REVISION AND APPROVAL HISTORY

Date	Revision No.	Author and Approval
15.8.24	1	CNC Fertility Research Centre
21.10/24		Approved RHW BRGC
6.2.25	2	Ashlee Rea CNC IVF
17.2.25	2	Endorsed RHW BRGC

Appendix A:

Luteal Phase Support

Utrogestan ® Progesterone	Available in 200mg vaginal/rectal pessaries Administered as 200mg BD or TDS
Oripro ® Progesterone	Available in 200mg or 400mg vaginal/rectal pessaries Administered as daily or BD
Cyclogest ® Progesterone	Available as 400mg vaginal/rectal pessaries Administered as 400mg BD
Prolutex ® Progesterone Injection	Dispensed as 25mg SC or IM injection. Patients should be advised to administer SC Administered daily or on alternate days
Ovidrel ® Choriogonadotropin alpha	Dispensed as 250mcg pen Administered as '8 x clicks' or 83.3 mcg on day 3, 6 and 9 post ovulation

Appendix B:

Natural embryo transfer planning and luteal phase support commencement

Day of LH Surge	Start LPS	Day of planned transfer
Monday	Wednesday	Saturday
Tuesday	Thursday	Sunday
Wednesday	Friday	Monday
Thursday	Saturday	Tuesday
Friday	Sunday	Wednesday
Saturday	Monday	Thursday
Sunday	Tuesday	Friday

Appendix C:

Modified natural and OI/FSH cycles embryo transfer planning and luteal phase support commencement

hCG trigger ➡ LH Surge (+1) ➡ Ovulation (+2) + 5 days[1]

Day of trigger	Start LPS (1st dose to be administered in am)	Day of planned transfer
Monday	Thursday	Monday
Tuesday	Friday	Tuesday
Wednesday	Saturday	Wednesday
Thursday	Sunday	Thursday
Friday	Monday	Friday
Saturday	Tuesday	Saturday

Appendix D:

HRT cycle embryo transfer planning and luteal phase support commencement

120 hours of exogenous progesterone prior to embryo transfer or P + 5 days (embryo age)[1]

Day of planned transfer	Start Pessaries
Monday	Wednesday
Tuesday	Thursday
Wednesday	Friday
Thursday	Saturday
Friday	Sunday