

In Vitro Fertilization Orientation

Tripler Army Medical Center



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Important Information

- REI Nurses: 433-5925/5951
- *****Fertility Institute of Hawaii: 545-2800**
 - Please call to pre-register.
 - Please pay prior to cycle start
- Consents will be signed at FIH prior to your Oocyte retrieval

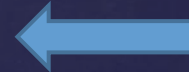
Information

℞ <https://www.reproductivefacts.org/news-and-publications/patient-fact-sheets-and-booklets/documents/fact-sheets-and-info-booklets/assisted-reproductive-technologies-booklet/>

Screening Before Starting IVF

- ⌘ Infectious Disease
 - ⌘ Hepatitis B/C, HIV, Syphilis (both partners)
- ⌘ Thyroid
- ⌘ Blood type and screen
- ⌘ Ovarian reserve (AMH or FSH/Estradiol)
- ⌘ Saline Infusion Ultrasound, Mock Transfer
- ⌘ Genetic Preconception Screening (covered later)

Expectations



Suppression

⌘ OCPs

- ⌘ Control timing
- ⌘ Synchronize the follicles
- ⌘ Suppress corpus luteum

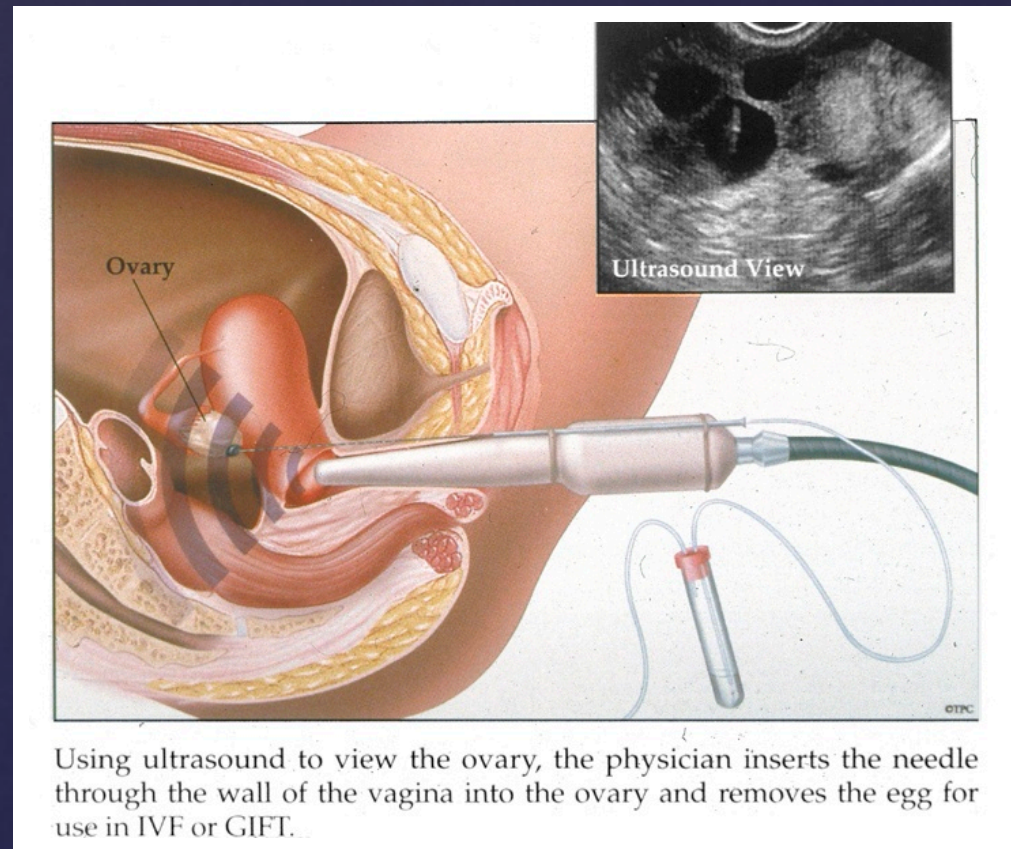
⌘ GnRH Agonists (Lupron)

⌘ GnRH Antagonists (Antagon)

} Prevent
premature
LH surge

Ovarian Hyperstimulation

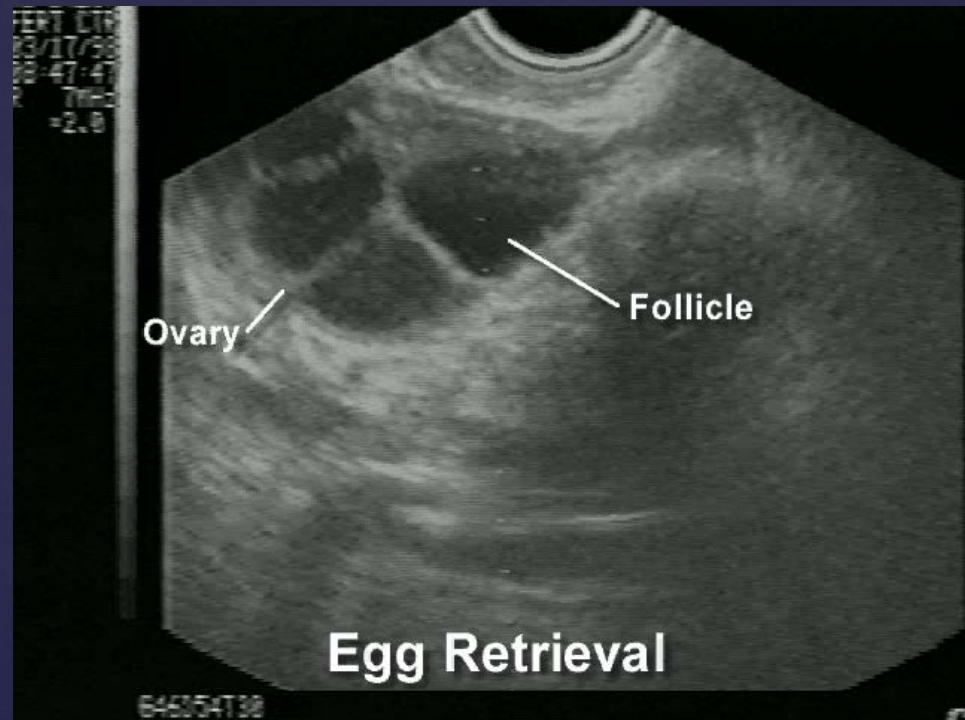
- Eggs are stimulated to grow with gonadotropins (SQ injections)
 - FSH: Follistim, Gonal-F,
 - hMG: Menopur
- Number and maturity of eggs - assessed by vaginal ultrasound/ estradiol level



Transvaginal Ultrasound

Oocyte (Egg) Retrieval

- Eggs are retrieved when follicles of sufficient number and size
- **Timed precisely 36 hours after hCG or Lupron injection**
- Retrieval is performed transvaginally under ultrasound guidance
- Sedation is used for pain control
- Outpatient procedure

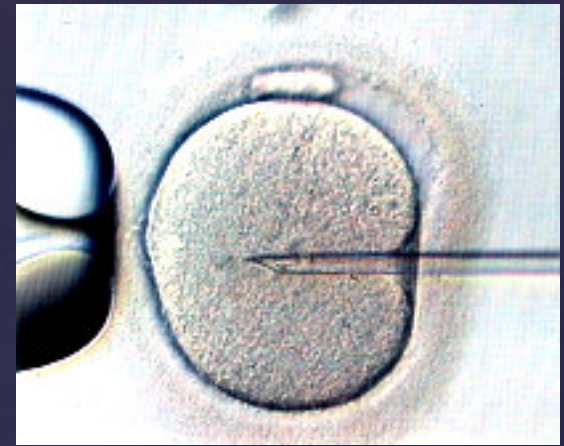


Sperm

- Obtained by masturbation on day of egg retrieval
 - If anticipate difficulty with collection or production, should consider freezing a specimen as backup (or having donor backup)
- For couples undergoing IVF while husband deployed, a frozen specimen(s) is thawed on day of egg retrieval
- For men with absent sperm, a sperm retrieval procedure (TESA) or donor sperm may be necessary



Fertilization



- **As many oocytes as possible given ovarian response to stimulation will be retrieved and you will be informed on the day of the procedure as to this number.**
- **Standard insemination or ICSI**
- **If concern exists regarding the number of oocytes to inseminate, you may specify the limit.**



Intracytoplasmic Sperm Injection

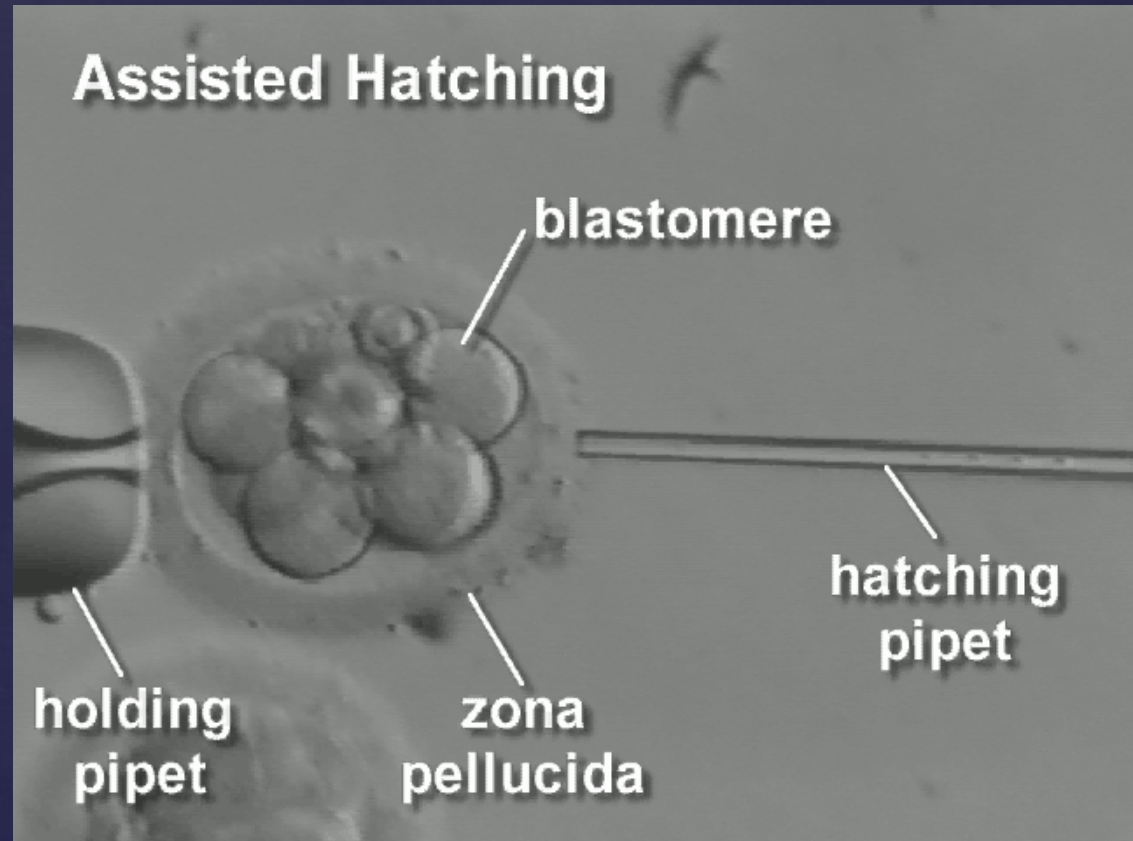
- Indications:
 - Required: azoospermia
 - Recommended:
 - Asthenozoospermia (<20%)
 - Oligospermia (< 10 M/cc)
 - Teratozoospermia (< 4%)
 - Prior IVF fertilization failure
 - Use of frozen sperm
- If semen specimen on day of egg retrieval is compromised, may be recommended that morning.



https://www.youtube.com/watch?v=VFR_4J9QCQE

Assisted Hatching

- Mechanism to facilitate hatching of embryos
- Using laser pulse or enzyme, a small hole is created in the shell of the embryo prior to transfer to the uterus
- Typically considered in situations that predispose to a thicker, harder shell such as age ≥ 38 years, previously unsuccessful IVF cycle or embryologist observation of thickened shell in vitro.

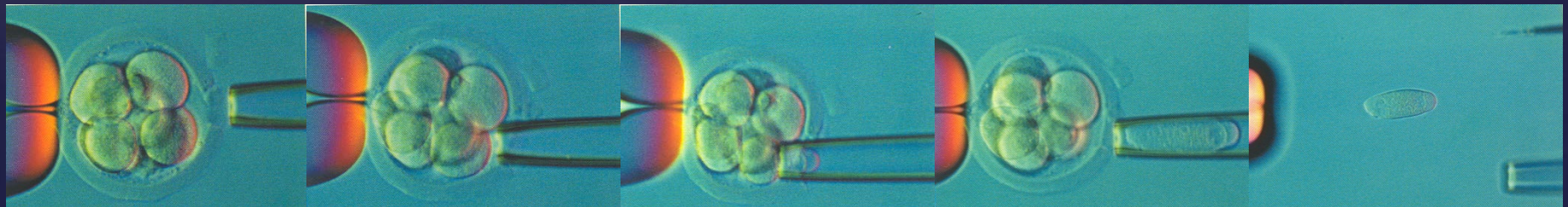


Genetic Screening

- ⌘ The American College of Obstetrics and Gynecology, along with the American College of Medical Genetics and Genomics, recommend all patients be tested for:
 - ⌘ Cystic Fibrosis
 - ⌘ Spinal Muscular Atrophy
- ⌘ In addition, we screen specific ethnicities for further syndromes (Jewish and eastern European).

Preimplantation Genetic Testing (PGT)

- Introduced in 1990 as an experimental procedure. Now widespread and readily accessible.
- PGT involves embryo biopsy at the cleavage (day 3) stage, with transfer of unaffected embryo(s) at the blastocyst (day 5) stage or in a frozen embryo transfer cycle.
- PGT is typically considered in situations where familial genetic disorder exists (i.e. Huntington disease) or focused on identifying embryos with normal chromosome number



Consents

& We can not:

- ∅ retrieve oocytes

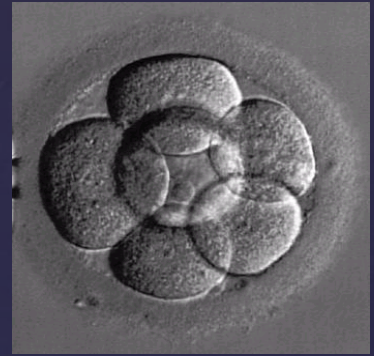
- ∅ fertilize with sperm

- ∅ and make and/or freeze embryos- without your consent!

& If you are planning PGT, let us know your plans as early as possible!

& Consents will be signed the day of the egg retrieval at FIH

Grading of Embryos



- On day 1 post-retrieval the eggs are checked for fertilization.
- Based on the number of fertilized eggs retrieved, your physician will make a recommendation for a day 3 versus day 5 transfer.
- Once the embryos are in culture they are not retrieved from the incubator until the day of transfer
- Grading assists to determine:
 - Which embryo to transfer
 - Number of embryos to transfer
- Grading does not:
 - Correlate with number of chromosomes
 - Correlate with health and ability of child

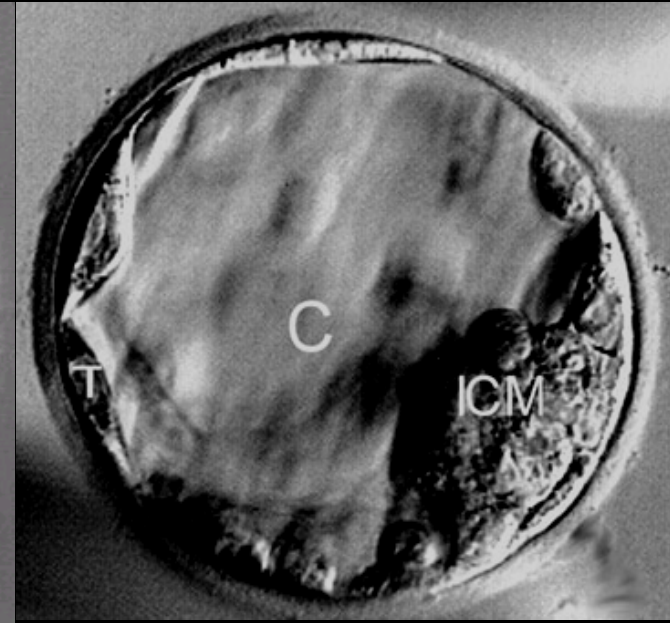
Embryo development



**Zygote
(Fertilized Egg)**



**Day 3 Embryo
(Cleavage Stage)**



**Day 5 Embryo
(Blastocyst)**

Advancing embryo development

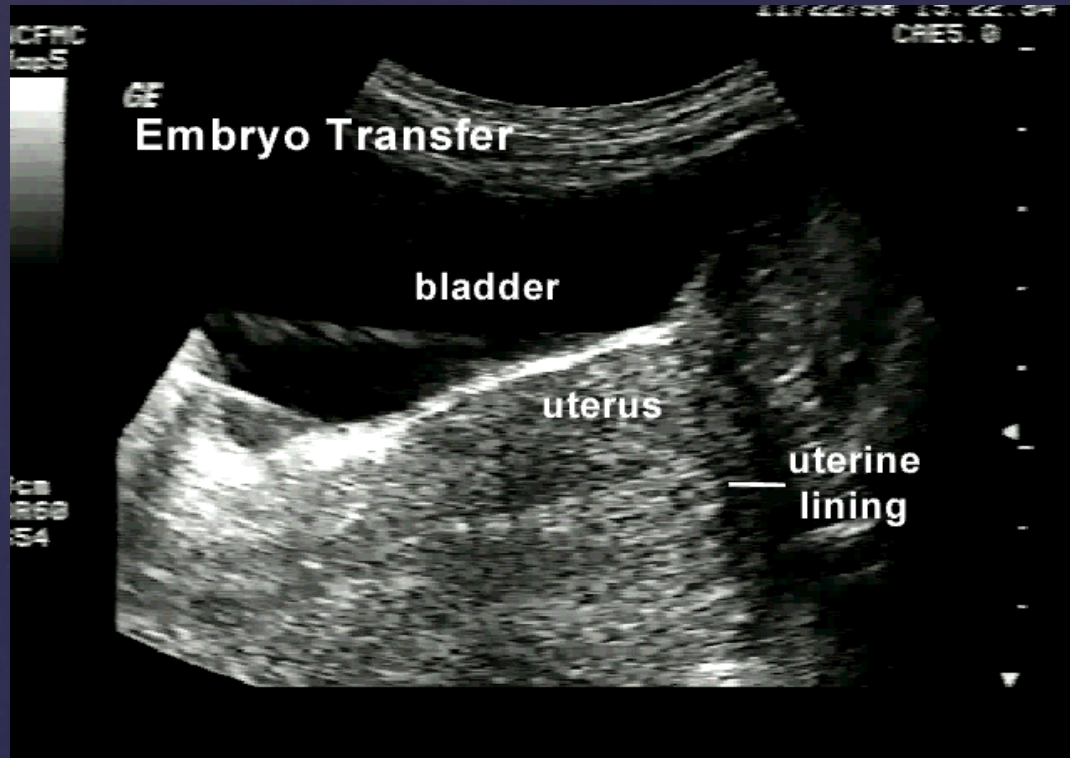
Growing to Blastocyst

- No guarantee that any embryos will survive
- Higher implantation rate than day 3 embryo
- Transfer of only one or two embryos
- Allows determination of which excess embryos are more suitable for cryopreservation

Human Blastocysts



Embryo Transfer Technique



- Clinic procedure
- Ultrasound guidance improves embryo implantation
- Requires full bladder

Number of embryos to transfer - summary

- So how many embryos get transferred?
 - Embryo quality
 - PGT
 - Embryo day
 - Prior history
 - Maternal age
 - Desires and concerns of the couple
 - Thoughts regarding MFR

Guidance on the limits to the number of embryos to transfer: a committee opinion

Practice Committee of the American Society for Reproductive Medicine, and the Practice Committee of the Society for Assisted Reproductive Technology

American Society for Reproductive Medicine; and Society for Assisted Reproductive Technology, Birmingham, Alabama

TABLE 1

Recommendations for the limit to the number of embryos to transfer.

	Age (y)			
Prognosis	< 35	35–37	38–40	41–42
Cleavage-stage embryos ^a				
Euploid	1	1	1	1
Other favorable ^b	1	1	≤3	≤4
All others	≤2	≤3	≤4	≤5
Blastocysts ^a				
Euploid	1	1	1	1
Other favorable ^b	1	1	≤2	≤3
All others	≤2	≤2	≤3	≤3

^a See text for more complete explanations.

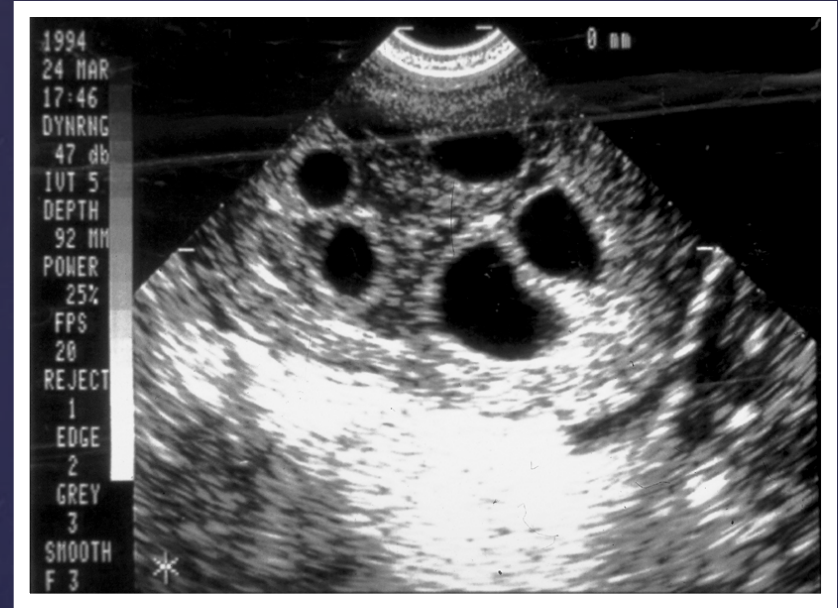
^b Other favorable = Any ONE of these criteria: *Fresh cycle*: expectation of 1 or more high-quality embryos available for cryopreservation, or previous live birth after an IVF cycle; *FET cycle*: availability of vitrified day-5 or day-6 blastocysts, euploid embryos, 1st FET cycle, or previous live birth after an IVF cycle.

Please note: Justification for transferring additional embryos beyond recommended limits should be clearly documented in the patient's medical record.

ASRM. Limits on number of embryos to transfer. *Fertil Steril* 2017.

Embryo Transfer – minimizing the risk of multiple gestation

- ASRM Guidelines (2017)
 - Under 35: no more than 1 embryos
 - 35 to 37: no more than 1 embryos
 - 38 to 40: no more than 3 embryos
 - Over 40: no more than 4 embryos
 - These guidelines pertain to patients with the most favorable prognosis. For other patients, transfer of more than that specified may be considered.
- Increasing trend toward single embryo/blastocyst transfer



Sonogram depicting uterus with five gestational sacs.

Maternal Complications of Multiple Gestation

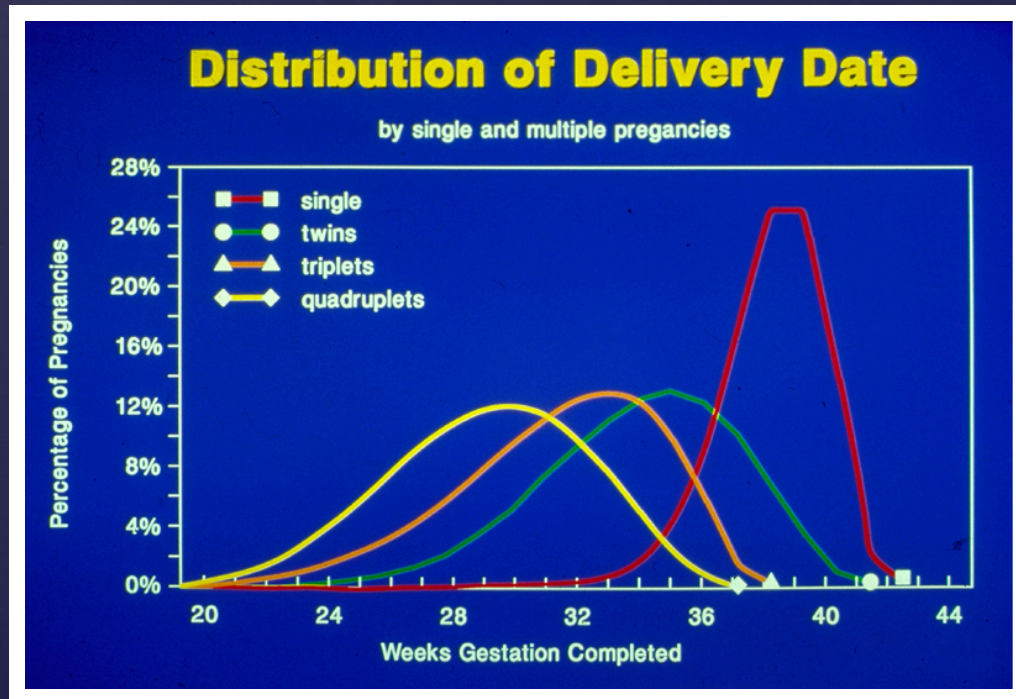
- Hypertension
- Gestational Diabetes
- Polyhydramnios
- Anemia
- Preterm labor and delivery
- Postpartum hemorrhage
- Bed rest and hospitalization
- Cesarean Delivery

Fetal Complications of Multiple Gestation

- ⌘ Respiratory distress
- ⌘ Low birth weight
- ⌘ Gastrointestinal problems
- ⌘ Prolonged admission to NICU
- ⌘ Severe prematurity
- ⌘ Blindness, deafness
- ⌘ Cerebral palsy
- ⌘ Death

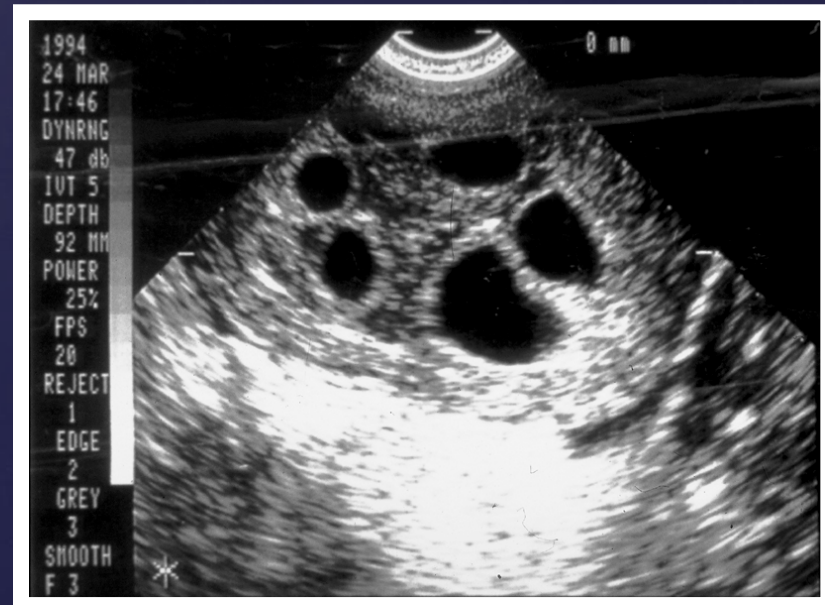
How many embryos to transfer – impact of multiple gestation

- Associated with pregnancy loss, pre-term birth, cesarean section, long term maternal bed rest, maternal diabetes and hypertension, long term health consequences for the children including cerebral palsy and birth defects



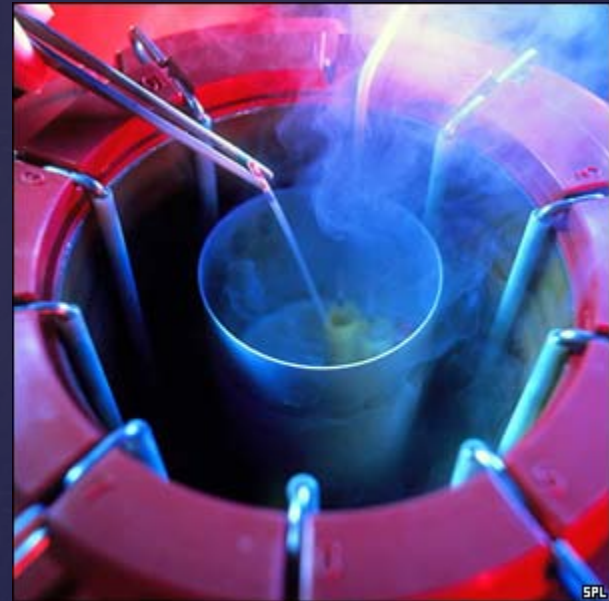
Multi-fetal reduction

- Reduction of high-order multiple pregnancy to twins or singleton
- Not done at military facility and not reimbursable
- Miscarriage rate approximately 10%



Embryo Cryopreservation

- Excess embryos beyond number transferred can be cryopreserved for later use.
- May freeze at various stages, but blastocyst is preferable
- May be stored in liquid nitrogen for an indefinite period.
- Cycles using thawed embryos do not require injections



Why consider frozen transfer?

[Fertil Steril](#). 2013 Jan;99(1):156-62. doi: 10.1016/j.fertnstert.2012.09.003. Epub 2012 Oct 3.

Fresh embryo transfer versus frozen embryo transfer in in vitro fertilization cycles: a systematic review and meta-analysis.

[Roque M¹](#), [Lattes K](#), [Serra S](#), [Solà I](#), [Geber S](#), [Carreras R](#), [Checa MA](#).

Author information

Abstract

OBJECTIVE: To examine the available evidence to assess if cryopreservation of all embryos and subsequent frozen embryo transfer (FET) results in better outcomes compared with fresh transfer.

DESIGN: Systematic review and meta-analysis.

SETTING: Centers for reproductive care.

PATIENT(S): Infertility patient(s).

INTERVENTION(S): An exhaustive electronic literature search in MEDLINE, EMBASE, and the Cochrane Library was performed through December 2011. We included randomized clinical trials comparing outcomes of IVF cycles between fresh and frozen embryo transfers.

MAIN OUTCOME MEASURE(S): ~~The outcomes of interest were ongoing pregnancy rate, clinical pregnancy rate, and miscarriage.~~

RESULT(S): We included three trials accounting for 633 cycles in women aged 27-33 years. Data analysis showed that FET resulted in significantly higher ongoing pregnancy rates and clinical pregnancy rates.

CONCLUSION(S): Our results suggest that there is evidence that IVF outcomes may be improved by performing FET compared with fresh embryo transfer. This could be explained by a better embryo-endometrium synchrony achieved with endometrium preparation cycles.

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Definitive Reasons to Freeze All

⌘ Ovarian Hyperstimulation

- ⌘ Patients with risk for hyperstimulation (Elevated estradiol levels >5K, more than 30 oocytes retrieved)

⌘ Polycystic Ovary Syndrome (NEJM)

⌘ Elevated progesterone the day of HCG trigger

- Well studied- this disturbs the window of implantation
- It is our recommendation that all couples consider a frozen cycle

Risks

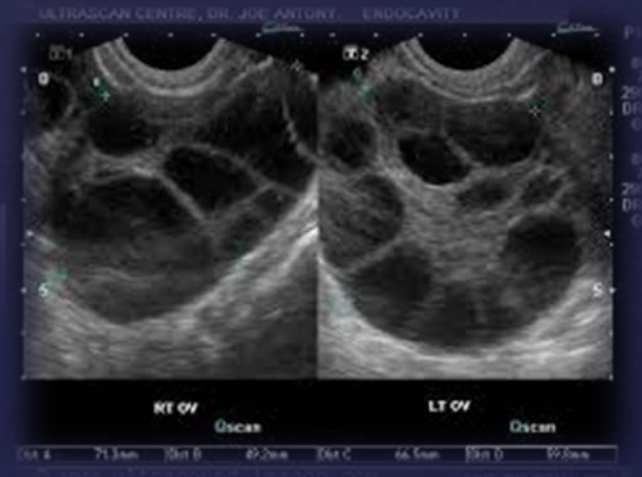


Risks of In-Vitro Fertilization (IVF and ICSI)

- ⌘ Risk of birth defects in the general population is 2-3% and is slightly higher among infertile patients (2.6 – 3.9%)
- ⌘ ICSI may also increase risk of birth defects and sex chromosome abnormalities (0.8 – 1.0% vs 0.2% in general population)
- ⌘ Rare conditions called imprinting disorders may also be higher
- ⌘ Increase rates of obstetrical complications

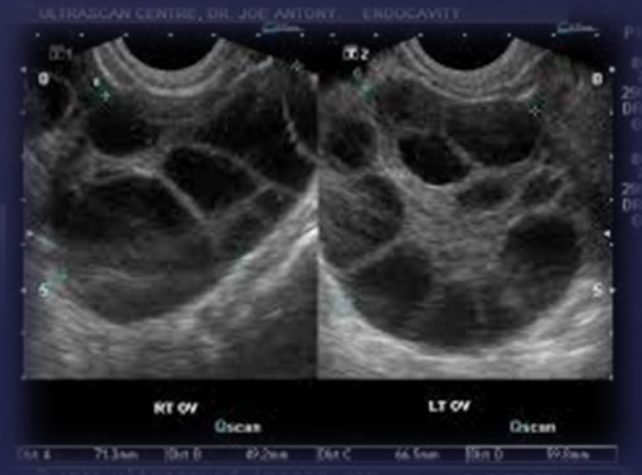
Risks of Ovarian Stimulation

- Severe ovarian hyperstimulation syndrome (OHSS)
 - Occurs in 1-2% of cases
- Fluid problems
 - May require removal with needle
 - May lead to kidney failure
- Blood clots
- Postponement of embryo transfer



Risks of Ovarian Stimulation

- Ovarian torsion
 - Large ovary may twist and block blood supply
 - Could affect future fertility
- Increase in risk of ovarian cancer
 - Controversial
 - Current data does not support
- Cancellation

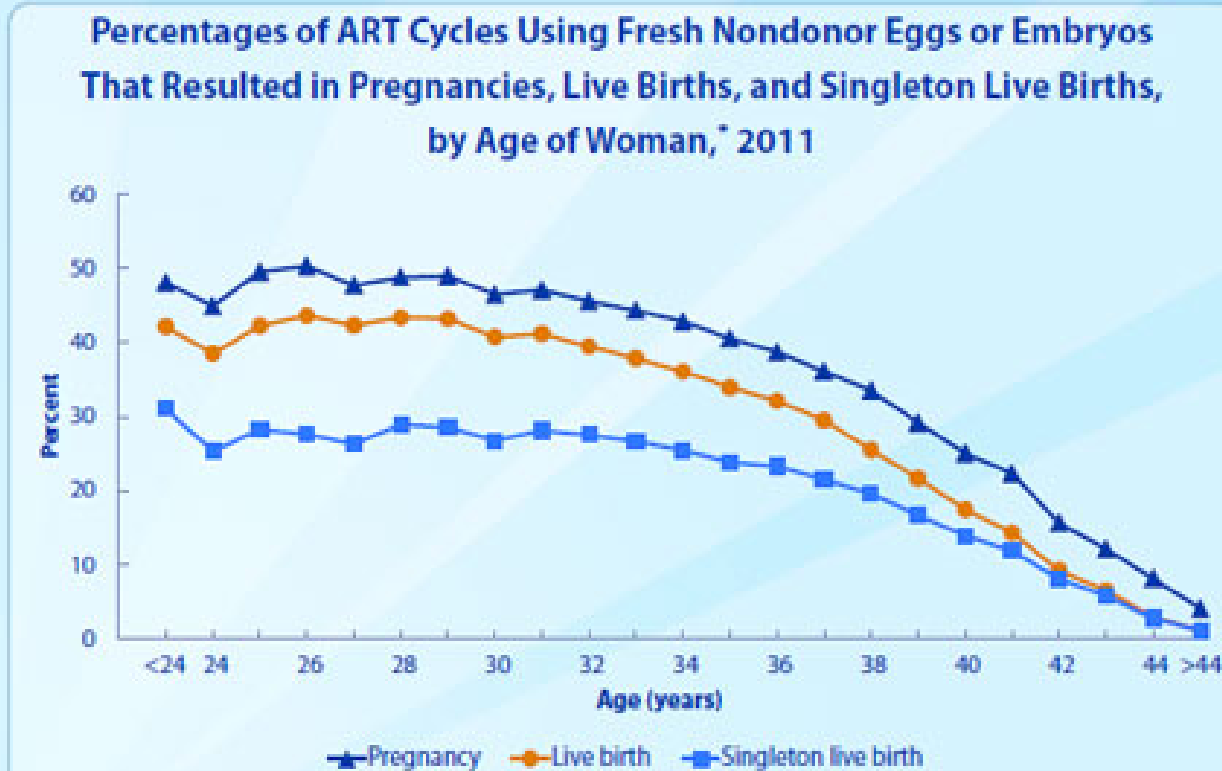


Risk of Oocyte (Egg) Retrieval

- Surgical
 - Bleeding
 - Infection
 - Damage to adjacent organs
- Anesthesia
- Failure to obtain oocytes
 - Reported up to 5%
 - Usually associated with error in injection of hCG



Impact of Age on Pregnancy Rates



National Center for Chronic Disease Prevention and Health Promotion
Division of Reproductive Health



TAMC
Pregnancy Rate
2018-2019
= 66%



Cancellation Option

- Fewer than 4 follicles for IVF cases
- Estradiol level < 500 on day 8-10 of stimulation
- If cancelled due to poor stimulation, minimal cost is incurred
- Options if cancellation occurs:
 - Repeat with a different IVF protocol
 - Recommend donor oocyte/embryo program or adoption

Financial Obligation

Fertility Institute of Hawaii 545-2800

+ cryopreservation

□ IVF \$ 4397.90 (\$5968.58)

□ ICSI \$ 5759.16 (\$7329.84)

□ Cryopreservation \$ 1570.68

□ Cancellation (pre- ER) \$ no charge

□ Cancellation (post- ER) \$ 2898.03

□ Embryo storage \$ 628.33

□ FET \$ 1870.68

□ PGT \$ 5235.60

□ *****Please call and schedule payment!*****

SOME THINGS TO REMEMBER

- Ask questions!
- Do not stop any medication unless you are instructed
- Do not take any NSAIDs (Motrin, Advil, Aleve, Ibuprofen, or aspirin)- Tylenol is ok😊
- ⌘ If you smoke: STOP
⌘(Both partners please)

SOME THINGS TO REMEMBER

- ⌘ After stopping the OCP's you will have a period in 2 to 4 days
- ⌘ We may need to see you frequently, please be available
- ⌘ Make sure you have enough medication to last at least 2 days each time you come in
- ⌘ Take the hCG shot within 10 minutes of the time instructed

SOME THINGS TO REMEMBER

- Husbands should not use hot tubs/saunas, and should ejaculate at least 2 days prior to retrieval
- Let us know in advance if you anticipate a problem with collection on retrieval day
- Exercise is allowed in moderation

SOME THINGS TO REMEMBER

- Most problems are not emergencies
 - ▣ Ask when you come in for ultrasounds
 - ▣ Call between 0800 and 1530.
 - ▣ Go to ER on weekends or nights
- Go to laboratory before your appointment for blood work
- If spouse will not be present for retrieval AND/OR transfer, you will need a Power of Attorney

Questions?

