INFERTILITY & SOCIAL EGG FREEZING

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Disclosures

None
Objectives

1. Fertility vs. Infertility
2. Basic workup for infertility
3. Ovarian reserve testing
4. Age related infertility
5. Social egg freezing

Definition

Infertility
- Failure to conceive after 12 months of unprotected intercourse
- Affects 15% of couples

Most conceive in 3 months

**Infertility**

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- Affects 15% of couples

**Most conceive in 3 months**

**Frequency of intercourse**

- Study of 221 couples:
  - Every day (37%) *
  - Every other day (33%) **NSD**
  - Weekly (15%) 


**Infertility: When to investigate early?**

1. **AGE**
   - > 35, after 6 mo
   - > 40, immediately

2. **Irregular cycles**
   - PCOS
   - Perimenopause
   - Endocrine disease

3. **Male factor**

4. **Tubal risk factors**
   - PID
   - Ectopic
   - Pelvic surgery
   - Endometriosis
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Basic workup for infertility

Eggs & Ovulation
- Age, d3 FSH, AMH
- Regular period (<35d), d21 progesterone > 10nmol/L, OPK

Uterus & Tubes
- HSG

Sperm
- Semen analysis
- Isolated low morphology of little importance
Sperm washing for analysis

Pre-wash

Post-wash

Causes of infertility

Clinical Gynecological Endocrinology, Fritz&Speroff, 8th ed.

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Ovarian reserve

- Technically it is the number of oogonia (eggs) remaining (in primordial follicles)
- We test ‘functional’ ovarian reserve by assessing hormone responsive pre-antral and antral follicles
- Function ovarian reserve provides a reasonable estimate of ‘true’ ovarian reserve

What is ‘normal’ ovarian reserve?

Day 3 FSH  |  Antral Follicle Count  |  AMH

FSH < 7 – 10IU/L  |  AFC > 7  |  AMH > 8pmol/L

* normals are highly age-dependent

Clinical Gynecological Endocrinology, Fritz&Speroff, 8th ed., Fertility and Sterility. Elsevier; 2008 Apr;89(4):868–78,
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Anti-Müllerian Hormone

- AMH throughout the lifespan in women
- Follicular gatekeeper

![Graph showing serum AMH data](image)

*Figure 1. Serum AMH data. The red line is the model that best fits the 3,260 datapoints shown as triangles. The coefficient of determination, $r^2$, is 0.34, indicating that 34% of variation in serum AMH concentrations is due to age alone. Peak serum AMH is at 24.5 years.*


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Anti-Müllerian Hormone

- Produced by pre-antral and antral follicles
  - NOT by the dominant follicle
  - Constant throughout the cycle


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Should you order AMH?

› AMH is **most commonly useful** for:
  - IVF dosing of gonadotropins
  - Patient expectations (IVF egg number)
  - Pre/Post ovarian surgery or chemotherapy

› Any doctor can order AMH from LifeLabs
  - 70$
  - No appointment needed
  - Results within 5 days

› Valid **any day** of the cycle
  - Slightly lower in OCP-users, pregnancy, post-partum, some ethnicities
  - Not consistently influenced by smoking, vitamin D deficiency, physical exercise, alcohol use, age at menarche, socio-economic status

AMH < 8pmol/L is low
High AMH ≠ PCOS

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Age-related infertility

Why is age such a problem?

- Women are having children later in life
- BC has the highest age of first birth in the country
  - 30.8 years
  - versus 30.5y in Ontario and 25.4y in Nunavut

British Columbia Vital Statistics Agency. [http://www2.gov.bc.ca/gov/content/life-events/statistics-reports/annual-reports/2011](http://www2.gov.bc.ca/gov/content/life-events/statistics-reports/annual-reports/2011)

Reasons for delayed childbearing

- #1 = lack of a partner
- Education
- Professional pursuits
- Personal
- Financial
- Circumstances

Hodes-Wertz, B et al. Fertil Steril 2013;100:1343

Costs of waiting:
1. Infertility
2. Miscarriage
3. Aneuploidy
What happens as eggs get older?

1. There are fewer eggs to choose from

![Graph showing decrease in total NGF as age increases](image)


What happens as eggs get older?

2. The eggs do not work as well!
   - Aneuploidy
   - E.g. meiotic spindle, mitochondria

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Number of subjects</th>
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<tbody>
<tr>
<td>0-1</td>
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<td>45-51</td>
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What should happen vs. Nondisjunction

- 21 – 35 years: 15-20%
- 40 years: 40-50%
- 45 years: 80-90%

Embryo aneuploidy increases with age


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Oocyte cryopreservation

- Egg freezing is “...a potential bridge during the gap between reproductive prime and when a woman is realistically ‘ready’ to have children.”

- Social egg freezing
  - Cryopreservation of mature oocytes on an elective basis for the purpose of delayed childbearing
  - First birth from a cryopreserved oocyte in 1986


Egg freezing – how does it work?

- Patients undergo ovarian stimulation just like an IVF cycle
  - Can leave IUD in situ
  - Sometimes we pre-medicate with the OCP

- Subcutaneous injections of FSH/LH for 8-12 days
- Ultrasound every other day at 730am

- Egg retrieval
  - 5 – 10 minute procedure
  - Conscious sedation
  - Patients need a ride home
  - Bloating is the #1 side effect

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Egg freezing technology

- Vitrification = ‘flash freezing’
  - Glass-like solidification

- Eggs are very delicate!

- LH surge: Prophase meiosis I $\rightarrow$ Metaphase of meiosis II

Oocytes are unique!

- Spherical
- Single cell (i.e. no room for error)
- High water content
- Low surface-area to volume ratio

- Vitification: “the new way”
- Cryopreservation without ice crystals
- -23 000°C/min

Egg freezing is safe

- 2014
  - 804 pregnancies from frozen eggs vs. 996 pregnancies fresh eggs IVF
  - 12.4% own oocytes, 85% donation

- No difference in: OB outcomes
  - GDM, hypertension, preterm birth, cholestasis, anemia

- No difference in perinatal outcomes
  - Gestational age at delivery
  - Preterm birth
  - APGAR scores
  - Birth defects
  - NICU admission
  - Perinatal mortality

- Only significant differences: Fewer UTIs, more invasive procedures (CVS or Amnio)

How well does it work?

- Elective egg freezing review (2016):
  - 1468 women who froze eggs
  - Mean age 37.7 years
  - 137 patients returned to use their eggs (9%)

Egg survival rate 85.2%

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1283 vitrified eggs (Doyle et. al. 2016)

128 IVF cycles
  ▶ Elective, lack of sperm, limiting fertilization

Egg-to-baby rate 6.4%

Frozen eggs compared to fresh eggs in autologous cycles had a similar live birth rate (39% vs 35%)
How well does it work?

How many eggs is ideal?

2017 prediction model

![Graph showing the likelihood of successful embryo retrieval based on age.](image)


Uterine aging

Can fertilize and transfer eggs until **age 50**

![Graph showing the percentage of successful embryo transfers by age.](image)
Are women happy?

- 201 women interviewed after egg freezing
- Scored by “DRS” Decision Regret Score
  - 0 = none, 100 = strong regret
- Median DRS score was 0, mean was 10
- Conclusion: low risk of regret
  - Those who did experience regret attributed it most commonly to low egg numbers frozen

Fertil Steril May 2018. epub. PMID 29807657

Egg freezing: Points of caution

- There is no number of eggs (or embryos) we can freeze to guarantee a live birth
- The *ideal* way to conceive is naturally!
- This is an evolving technology
- Social implications – debated!
Costs of social egg freezing

- $7000 + medications ($3000 – 5000 if no extended drug plan)
- Annual storage $250
- Most cost effective at 37 according to one study
- Biologically optimal at age 34 or lower


Infertility & Egg freezing conclusions

1. AGE
   - > 35, after 6 mo
   - > 40, immediately
2. Work up
   - Day 3 FSH, AMH
   - HSG
   - Semen analysis
3. AMH
   - 70$ at Lifelabs
   - Accurate but age-specific
4. Delayed childbearing
   - Infertility
   - Miscarriage
   - Aneuploidy
5. Egg freezing
   - Safe
   - Effective
   - Not a guarantee!
THANK YOU FOR COMING!
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So really, how well does it work?

- Compared to IVF with fresh eggs
- 2014 aggregate data from 31 Canadian IVF clinics

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