Oocyte Cryopreservation

- Experimental option
- Offer to single cancer patients with no male partner/or those who do not wish to use a sperm donor
- Requires ovarian stimulation
- Many cancer patients may not have time to complete a stimulated cycle
Oocyte Cryopreservation

- 1986 – First human live birth from cryopreserved oocytes
- Early results disappointing
  - Low survival, fertilization, pregnancy rates
  - Very fragile meiotic spindle
  - Ice crystals can form and cause damage to spindle apparatus
  - Mature oocytes are extremely fragile due to their large size, high water content and chromosome arrangement


Recent Oocyte Cryopreservation Technology

- Better post-thaw survival, fertilization, pregnancy rates
- ICSI has overcome the zona hardening caused by the freezing process preventing fertilization
- 1997 – First human live birth after transferring embryos generated by ICSI of cryopreserved oocytes*
- Estimated > 200 babies have been born from previously frozen oocytes & # of pts with frozen oocytes is > 1000


Different Cryopreservation Protocols Available

- **Slow freeze-rapid thaw method**
  - Most commonly used and achieved the first pregnancy worldwide
  - Estimated live-birth rate per oocyte thawed 2%*

- **Vitrification**
  - Highly concentrated cryoprotectant solution with a high cooling rate used to achieve a glassy, solid, state without causing ice formation
  - Easier and less expensive
  - Does not require a programmable freezer
  - Improved post-thaw survival and fertilization rate and live births have been achieved by vitrification of mature oocytes using ethylene glycol and dimethyl sulfoxide as cryoprotectants
  - Estimated live-birth rate per oocyte thawed 4%*

Clinical Utility of Oocyte Cryopreservation
- Primarily offered to cancer patients
- Women undergoing ART with extra eggs that prefer not to create embryos
- Women who are interested in deferring reproductive aging

Recent Efficacy of Oocyte Freezing Methods Compared
- Offered to couples doing IVF with > 9 oocytes
- If no pregnancy in fresh cycle, use cryopreserved oocytes
  - Oocytes frozen in 165 cases; 63 choose to use oocytes
  - 66% (SR-F) - 73% (V) survived & fertilized with ICSI (Randomly chosen for SR-F or V)
  - Pregnancy success 18% (SR-F) – 34 % (V)
  - Needed 21 (V) oocytes vs 45 (SR-F) oocytes for clinical pregnancy

Safety of Oocyte Freezing
- 149 pregnancies observed; 89 pregnancies resulted in live birth of 105 babies conceived with frozen oocytes (SR-F)
- Average gestation 38.9 weeks
- Average weight 3.35 kg for singletons and 2.6 kg for twins
- 35 pregnancies ended in sp ab
- 1 pregnancy aborted for Trisomy 21
- 2 of 105 babies born had malformations
Health of Children Born from Cryopreserved Oocytes

- Literature survey
- 272 clinical pregnancies up to July 2006
- 93.8% normal results for eggs that had PGD of second polar body and karyotyping after fertilization
- 51 sp ab, 2 ectopics, 156 deliveries of 197 babies & 63 ongoing pregnancies
- 69.5% pts. reported and 99.3% of babies were healthy
- F/u reported at 6 months to 3 yrs for 31 % of children—all developing normally
- One twin was born with a congenital anomaly


Rate of Ovarian Failure After Chemotherapy

- 168 young patients with various cancer following chemotherapy
  - Failure rate for entire group was 34%
  - **Age predicted highest chance of ovarian failure**
  - All patients treated with combination chemotherapy
  - Alkylating agents imposed highest risk
  - AML 15%; nonHodgkin’s lymphoma 44%; Hodgkin’s disease 32%; breast cancer 31%


Partial Ovarian Injury

- Patients’ menstrual cycle may continue after therapy completed
- Destruction of primordial follicles is not “all or none” -- dose related, especially with cyclophosphamide
- High risk for premature menopause!
- Recommended that patients who regain ovarian function do not delay childbearing!
  - Should try after a few years of disease-free intervals, but not less than 6-12 after treatment

Effect of Radiation Dose and Age on Ovarian Function.

<table>
<thead>
<tr>
<th>Ovarian cGy</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>No deleterious effect</td>
</tr>
<tr>
<td>150</td>
<td>No deleterious effect in young women; some risk for sterilization in women older than 40</td>
</tr>
<tr>
<td>250-500</td>
<td>In women aged 15–40, 60% permanently sterilized; remainder may suffer temporary amenorrhea. In women older than 40, 100% permanently sterilized</td>
</tr>
<tr>
<td>500-800</td>
<td>In women aged 15–40, 60%–70% permanently sterilized; remainder may experience temporary amenorrhea. No data available for women over 40</td>
</tr>
<tr>
<td>&gt;800</td>
<td>100% permanently sterilized</td>
</tr>
</tbody>
</table>

Damewood MD, Grochow LB. Prospects for fertility after chemotherapy or radiation for neoplastic disease. Fertil Steril 1986;45:443-459