PRE-CONGRESS COURSE 1

Fertility preservation - The next frontier.

Paramedical Group
London - UK, 7 July 2013
Fertility preservation - The next frontier

London, United Kingdom
7 July 2013

Organised by
The ESHRE Paramedical Group
Contents

Course coordinators, course description and target audience  
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Speakers’ contributions

Role of the nurse in England - Rebecca Goulding - United Kingdom  
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Oocyt Cryopreservation – alternative technique to embryo freezing - Laura Francesca Rienzi - Italy  
Oocyte banking in an egg-donation programme - Elisabeth Clare Larsen - Denmark  
Oocyte cryopreservation: applications and outcomes in the U.S.A. - Nicole Noyes - U.S.A.  
Counseling for social freezing - Julie Nekkebroeck - Belgium  
Ethical issue of social freezing - Françoise Shenfield - United Kingdom  

Upcoming ESHRE Campus Courses  
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Course coordinators

Jolienke Schoonenberg-Pomper (The Netherlands) and Helle Bendtsen (Denmark)

Course description

An advanced course for nurses and lab technicians focussing on the different aspects of fertility preservation

Target audience

Nurses and lab technicians.
Scientific programme

Chairman: Helle Bendtsen - Denmark
Chairman: Helen J. Kendrew - United Kingdom

09:00 - 09:10 Introduction
Helle Bendtsen - Denmark

09:10 - 09:40 Role of the nurse in England
Rebecca Goulding - United Kingdom

09:40 - 09:50 Discussion

09:50 - 10:20 Risk of premature ovarian failure
Ina Beerendonk - The Netherlands

10:20 - 10:30 Discussion

10:30 - 11:00 Coffee break

11:00 - 11:25 Fertility preservation in women affected by malignant diseases; when (indication), and how (procedures)
Kirsten Louise Tryde Schmidt - Denmark

11:25 - 11:35 Discussion

11:35 - 12:00 Oocyt Cryopreservation – alternative technique to embryo freezing
Laura Francesca Rienzi - Italy

12:00 - 12:10 Discussion

12:10 - 12:30 Hands-on session vitrification- companies will show different vitrification devices for oocytes
Helle Bendtsen - Denmark

12:10 - 12:30 Hands-on session vitrification- companies will show different vitrification devices for oocytes
Cecilia Westin - Sweden

12:10 - 12:30 Hands-on session vitrification- companies will show different vitrification devices for oocytes
Yves Guns - Belgium

12:30 - 13:30 Lunch

13:30 - 14:05 Oocyte banking in an egg-donation programme
Elisabeth Clare Larsen - Denmark

14:05 - 14:15 Discussion

14:15 - 14:50 Oocyte cryopreservation: applications and outcomes in the U.S.A.
Nicole Noyes - U.S.A.

14:50 - 15:00 Discussion

15:00 - 15:30 Coffee break

15:30 - 16:00 Counseling for social freezing
Julie Nekkebroeck - Belgium

16:00 - 16:10 Discussion

16:10 - 16:40 Ethical issue of social freezing
Françoise Shenfield - United Kingdom

16:40 - 17:00 Discussion
The Role of the Nurse in England

Rebecca Goulding RGN BA Hons
Senior Fertility Sister

Chelsea Westminster Hospital NHS Foundation Trust
London United Kingdom

Learning Objectives

- Who we are and what we do
- Development
- Opportunities

How times have changed…
Introduction

• Definition of a nurse

* a person trained to look after sick or injured people

Oxford Dictionary (2001)

What is a Nurse?

• Trust

• Treat as individuals

• Maintain confidentiality

• Collaboration of care

What is a Nurse?

• Consent

• Professional boundaries

• Share information

• Work effectively
What is a Nurse?

- Delegate
- Manage risk
- Evidence
- Personal development

What is a Nurse?

- Documentation
- Integrity
- Problem solving
- Impartial
- Professional

The role of the Fertility Nurse

- Advocate
- Counsellor
- Performing clinical procedures
- Leadership and Management
The role of the Fertility Nurse

- Training and Education
- Ultrasound Scanning
- Prescribing
- Consulting

The role of the Fertility Nurse

- Quality Management and Audit
- Data Collection
- Risk Assessment
- Mentoring

The role of the Fertility Nurse

- Person Responsible
- Dignity and Respect
- Confidentiality
Super Nurse

Frantic Nurse

Development

’As a registered nurse, midwife or health visitor, you are professionally accountable for your practice’

'All nursing staff must be appropriately qualified and registered by the nursing and midwifery council'

- Working towards competencies
- Appropriate standards of clinical competence
- Able to provide evidence
- Suitably qualified
Competencies Tool

Collecting Evidence

Evidence
- Supervised practice
- Work based projects
- Practice developments/changes in practice
- Incident reporting
Evidence

- Reflective diaries/log books
- Assessments and appraisals
- Audit

Evidence

- Teaching sessions/posters
- Policy and protocol developments
- Standard operating procedures
- Patient feedback

Opportunities - Locally
Opportunities - Nationally

Opportunities - Internationally

Summary

- Training and updating essential
- Maintain competences
- Ability to acknowledge our limitations
Summary

- Opportunities are there
- Multi professional approach
- Show leadership and collaborative practice

Thank You

Rebecca.goulding@chelwest.nhs.uk
Useful Links

- www.rcn.org.uk
- www.hfea.gov.uk
- www.nmc-uk.org
- www.eshre.eu
- www.britishfertilitysociety.org.uk

References

Risk of premature ovarian failure

Ina Beerendonk, MD PhD
Gynaecologist in Reproductive Medicine

Department of Obstetrics & Gynaecology
Radboud University Nijmegen Medical Centre
Nijmegen - The Netherlands

Disclosures

No potential conflict of interest

Learning objectives

• To learn about who is at risk of POF
• To learn about the damaging effect of cancer treatment on female reproduction
• To provide information on how the expected amount of damage can be determined
• To discuss on what indications fertility preservation (FP) should be offered and in what form
Who is at risk of Premature Ovarian Failure (POF)?

All patients whose disease or its treatment may cause infertility and early menopause:

- Cancer patients
- Mutation carriers for certain types of cancer
- Patients with auto-immune diseases
- Patients undergoing bone marrow or stem cell transplantation
- MS patients receiving new generation treatments
- Patients with genetic mutations leading to loss of fertility and early menopause
Highest impact on fertility

- Alkylating agents
- Cranial / brain radiation
- Hormone sensitive tumors requiring castration
- Bone marrow and stem cell transplants
- Auto-immune diseases
- Genetic mutation
- Genetic mutations that predispose to cancer
- Chemotherapeutic agents that impact gametes

Ovarian function after radiotherapy

Depending on:
- Age of woman
- Type of radiation:
  - Pelvic / abdominal
  - Total body
  - Cranial
  - Doses

Ovarian function after radiotherapy

- 4 Gy 30% sterility in young women
- 4 Gy 100% sterility in women > 40 years
- LD50 human oocyte: < 2 Gy (Wallace et al, 2003)
Ovarian function after chemotherapy

Depending on:

- Age of woman
- Type of chemotherapy
- Total dose

Ovarian function after chemotherapy

- Alkylating agents most harmful
- Prepubertal ovaries least vulnerable
- Early menopause in the longer term

Other reproductive functions

- Puberty
- Sexual development
- Endocrine function
- Function uterus
Low risk

Less than 20% infertility

• AC in women 30–39 years
• CMF, CEF, or CAF x 6 cycles in women <30 years
• Nonalkylating chemotherapy: ABVD, CHOP, COP
• AC

Adapted from the 2006 ASCO recommendations on fertility preservation in cancer patients

No risk

• Radioactive iodine
• Methotrexate / 5-fluorouracil
• Vincristine

Adapted from the 2006 ASCO recommendations on fertility preservation in cancer patients

Unknown risk

• Paclitaxel, docetaxel (taxanes used in AC protocols)
• Oxaliplatin
• Irinotecan
• Bevacizumab
• Cetuximab
• Trastuzumab
• Erlotinib
• Imatinib

Adapted from the 2006 ASCO recommendations on fertility preservation in cancer patients
Risk Calculator Fertile Hope

Risk Calculator: Women — Search by Cancer Type

The risk calculator information is based on large research projects that estimate rates of cancer in women ages 35 and younger. It is a tool to help you assess your risk of cancer based on your family history and personal health factors. The calculator provides estimates of your lifetime risk of developing certain cancers based on your specific family history and personal health factors. It is not intended to diagnose or treat any condition. It is not a substitute for medical advice. It is not designed to replace your healthcare provider’s advice or your personal health information. The information provided here is intended to be a general guide to help you understand your risk.

Example of Risk Calculator Fertile Hope

Search Result: Sarcoma

Degree of Risk: High Risk

— Any history of cancer (e.g., breast cancer, colorectal cancer, ovarian cancer)
— Total time on chemotherapy or radiation therapy
— Induction chemotherapy or radiation therapy
— Higher-dose chemotherapy or radiation therapy
— Higher cumulative dose

Fertility Preservation - Where Does It Fit?

Figure adapted from SaveMyFertility.org
Options calculator Fertile Hope

Indications

Overview:
- N = 59
- Age 4-44 years
- USA


Options for FP in women with cancer

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Method</th>
<th>Complications</th>
<th>Treatment</th>
<th>Success</th>
</tr>
</thead>
</table>
| Breast | &nbs
| Prostate | &nbs
| Gynecologic | &nbs
| Hematoi
| 1-2 cycles | &nbs
| Hormone therapy | &nbs
| Laparoscopic surgery | &nbs
| Chemotherapy | &nbs
| Ovarian transposition | &nbs
| Cryopreservation | &nbs
| Transposition | &nbs
| Ovarian grafting | &nbs

Summary

• Cancer and cancer treatment may have a high impact on female fertility
• Also benign diseases and their treatment may have a high impact
• Internet offers risk and options calculators for patients and professionals
• The risk of infertility and FP options should be discussed with all women at risk of POF
• Nowadays different kinds of FP are available for women at various ages

Bibliography

Articles

Websites
• www.oncofertility.northwestern.edu
• www.fertilehope.org
• www.savemyfertility.org
Fertility preservation in women affected by malignant diseases; when and how?

Kirsten Tryde Schmidt
M.D., Ph.D.
The Fertility Clinic, Rigshospitalet
Copenhagen University Hospital

Disclosure

- I have no conflict of interest in relation to this talk

Learning objectives

- At the conclusion of this presentation, participants should be able to:

  1. Identify those women at risk of ovarian failure due to cancer treatment
  2. Describe the different methods of fertility preservation in women
  3. Discuss the pro's and con's of the different methods
Options to preserve fertility

**Methods to shelter the ovary**
- Co-treatment with GnRH-a
- Ovarian transposition or shielding

**Methods to store gametes**
- IVF with vitrification of oocytes
- IVF with cryopreservation of embryos
- Cryopreservation of ovarian tissue

Gonadotoxicity of cancer treatment

**Chemotherapy:**
- Alkylating agents
- (Antimetabolites)
- (Plant alkaloids)
- (Taxanes)

**Radiation therapy:**
- Abdominal irradiation
- Cranial irradiation
- Craniospinal irradiation
- Total body irradiation

Who should be offered fertility preservation?

- Ideally, anyone at risk of loss of ovarian function

- Risk depends on
  - Age
  - Type of drugs used
  - Cumulative dose
  - Ovarian reserve of the patient

- Beware of contraindications
  - Is the patient too sick?
  - Are there anaesthetic contraindications?
  - Increased risk of bleeding or infection?
Co-treatment with a GnRH-a

- Non-invasive
- Low-cost
- Mechanism of action unknown
- Effect still questionable

More RCT’s are needed!

Transposition of the ovaries

- ‘Invented’ in the 50’s for cervical cancer pt.
- Ovaries are surgically moved out of field of radiation
- Scatter-radiation
- Side effects: chronic pain, vascular injury, ischemia, ovarian cysts, IVF to obtain a pregnancy

Woo and Viswanathan, 2009

IVF with cryostorage of oocytes or embryos

Vitrification of oocytes:
- Newer technique
- Results approaching those of embryo cryopreservation
- Ideal for single women and younger patients
- Takes 2-3 weeks

Cryopreservation of embryos:
- Well-known technique
- Good for patients in stable relationships
- Ethical issues in case of death of the patient
- Takes 2-3 weeks

IVM of immature oocytes or vitrification of immature oocytes is still experimental, few clinics offer this, low implantation- and delivery rates.
IVF protocols in breast cancer patients

Oktay et al, 2005

Tamoxifen protocol

GnRH-a

GnRH-ant

CD 2-3

OPU

150 rFSH + 40 mg Tamoxifen

3.8 embryos ± 0.8

Letrozole protocol

GnRH-a

GnRH-ant

CD 2-3

OPU

150 rFSH + 5 mg Letrozole

5.3 embryos ± 0.8

Cryopreservation of ovarian tissue

Tissue is put back

• Cancer

• POI

• Chemotherapy or radiation therapy

• Orthotopically

• Heterotopically

• Return of ovarian function

From 1999 to Feb 2013 591 patients have had ovarian tissue cryopreservation in Denmark

75 have died ~13%
Age-distribution amongst patients with cryopreserved ovarian tissue

<table>
<thead>
<tr>
<th>Age</th>
<th>0-4</th>
<th>5-9</th>
<th>10-14</th>
<th>15-19</th>
<th>20-24</th>
<th>25-29</th>
<th>30-34</th>
<th>&gt; 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>23</td>
<td>30</td>
<td>40</td>
<td>60</td>
<td>70</td>
<td>100</td>
<td>140</td>
<td>43</td>
</tr>
</tbody>
</table>

93 girls

Results from autotransplantation

- 22 patients have received autotransplantation a total of 31 times
- Thus, 9 patients have had an additional transplantation
- All have regained their ovarian function (mean 20 weeks) as seen by return of menses and antral follicles on ULS

Mean concentration of FSH IU/l ± SEM following transplantation of frozen/thawed ovarian tissue to 15 Danish women
Pregnancies in Danish women with autotransplanted ovarian tissue

- Nine women have obtained a total of 13 pregnancies
  - 2 biochemical (IVF)
  - 2 spontaneous abortions (IVF)
  - 2 induced abortion (spontaneous)
  - 3 ongoing pregnancies (2 IVF, 1 spontaneous)
  - 4 deliveries (2 IVF, 2 spontaneous)

<table>
<thead>
<tr>
<th>Rec. of ART cycles</th>
<th>Best result of IVF/ICSI</th>
<th>Duration of graft function (months) (1st/2nd transplantation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1 embryo transferred</td>
<td>45 / 25</td>
</tr>
<tr>
<td>10</td>
<td>2 biochemical pregnancies</td>
<td>88 – 34 –</td>
</tr>
<tr>
<td>12</td>
<td>1 clinical pregnancy</td>
<td>26 / 43</td>
</tr>
<tr>
<td>8</td>
<td>1 livebirth</td>
<td>15 / 64 –</td>
</tr>
<tr>
<td>1</td>
<td>1 livebirth</td>
<td>70 –</td>
</tr>
<tr>
<td>2</td>
<td>Follicles visible on ultrasound</td>
<td>7 / 0</td>
</tr>
<tr>
<td>14</td>
<td>1 embryo transferred</td>
<td>22 / 32</td>
</tr>
<tr>
<td>3</td>
<td>2 embryos transferred</td>
<td>42 –</td>
</tr>
<tr>
<td>7</td>
<td>1 oocyte aspirated</td>
<td>12 / N.A</td>
</tr>
<tr>
<td>10</td>
<td>5 embryos transferred</td>
<td>27 –</td>
</tr>
<tr>
<td>2</td>
<td>1 embryo transferred</td>
<td>27 –</td>
</tr>
<tr>
<td>Total 71</td>
<td></td>
<td>Live birth rate: 2/71= 3% per cycle</td>
</tr>
</tbody>
</table>

Schmidt et al., 2010

Relevance of different methods of fertility preservation

<table>
<thead>
<tr>
<th>Method</th>
<th>Pre-pubertal girl</th>
<th>Adolescent girl</th>
<th>Single woman</th>
<th>Woman with partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>GnRH-a</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Ovarian transposition</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Oocyte cryopreservation</td>
<td>[X]</td>
<td>X</td>
<td>[X]</td>
<td></td>
</tr>
<tr>
<td>Embryo cryopreservation</td>
<td>[X]</td>
<td></td>
<td>[X]</td>
<td></td>
</tr>
<tr>
<td>Ovarian tissue cryopreservation</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>
Conclusion

- Fertility preservation should be offered to women and girls with a risk of iatrogenic ovarian damage.
- Cryostorage of oocytes or embryos offers a possibility of a future pregnancy.
- Cryopreservation and autotransplantation of ovarian tissue restores the ovarian function in terms of resumption of a menstrual cycle.
- Pregnancies are still scarce but more and more are reported.

References


Learning objectives

1. Role of oocyte cryopreservation in ART
2. Cryopreserved oocytes laboratory performances
3. Clinical evidences of efficiency
4. Comparison between oocyte and embryo cryopreservation in the infertile population
5. Conclusion: oocyte cryopreservation can be considered a standard procedure in ART today?

I declare no conflict of interest related to this presentation

Oocyte cryopreservation has a key role

Oocyte cryopreservation is an emerging discipline that has already a key role in different applications:

- Fertility preservation for medical reasons
- Fertility preservation for social reasons
- Use of cryo-banked oocytes for egg donation
- Avoids the production of supernumerary embryos in IVF
- Accumulation of excess oocytes in IUI cycles
Oocyte cryopreservation was considered experimental. In contrast to preservation of male fertility, the techniques to preserve female fertility have only been recently developed. According to the most recent recommendations of the American Society for Reproductive Medicine (ASRM, 2006, 2008) and the American Society of Clinical Oncology (ASCO, 2006), embryo cryopreservation is the only established option for fertility preservation in female cancer patients, while the other methods are still considered experimental.

Today, not any more (ASRM guideline 2012)

Mature oocyte cryopreservation: a guideline

The Task Force of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology

Clinical evidences prove this
Why has it been so difficult?

- Cytoplasmic and cytoskeleton damage
- Oocyte ageing
- Zona pellucida hardening
- Membrane permeability
- Meiotic spindle depolymerization
- Polar body degeneration/fusion
- Impact on oocyte physiology

Timeline of principal evidences

2008: Efficiency in donation program not compromised with vitrification (Cobo et al., 2008; Nagy et al., 2008)
2008: The clinical pregnancy rate double with the introduction of vitrification (Tulandi, 2008; Cao et al., 2006; Smith et al., 2010 (RCT))
2010: Prospective randomized study with own sibling oocytes demonstrates the lab efficiency of the technique (RCT) (Rienzi et al., 2010)
2010: Cumulative ongoing pregnancy rate with oocyte vitrification in a standard infertility program (Ubaldi et al., 2010)
2010: Prospective randomized study with donor oocytes demonstrates clinical efficiency of the technique (RCT) (Cobo et al., 2011)
2011: Efficiency of oocytes vitrification in the infertile population (RCT) (Parmegiani et al., 2011)
2012: Multicentric longitudinal cohort study to confirm reproducibility (Rienzi et al., 2012)

Evidence from the Lab

Comparison of concomitant outcome achieved with fresh and cryopreserved donor oocytes vitrified by the Cryotop method

Evidence of early development of both normal chromosomally intact 8-celled embryos after NCM oogenesis: randomized single-oocyte study

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Evidence of development of both normal chromosomally intact 8-celled embryos after NCM oogenesis: randomized single-oocyte study
### Evidence from the Lab

<table>
<thead>
<tr>
<th>Evidence quality</th>
<th>Category</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Poor</td>
<td>1-2</td>
</tr>
<tr>
<td>Moderate</td>
<td>Fair</td>
<td>3-5</td>
</tr>
<tr>
<td>High</td>
<td>Good</td>
<td>6-10</td>
</tr>
</tbody>
</table>

### RCT and meta-analysis = evidence based medicine

#### Table 1: Effect of treatment on fertilization, pregnancy morphology, embryo development and implantation and pregnancy outcome

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Fertilization Rate</th>
<th>Pregnancy Rate</th>
<th>Embryo Development</th>
<th>Implantation Rate</th>
<th>Pregnancy Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug A</td>
<td>80%</td>
<td>50%</td>
<td>90%</td>
<td>75%</td>
<td>85%</td>
</tr>
<tr>
<td>Drug B</td>
<td>75%</td>
<td>45%</td>
<td>85%</td>
<td>60%</td>
<td>65%</td>
</tr>
</tbody>
</table>

### Clinical evidence: infertile population

#### Table 2: Clinical outcomes

<table>
<thead>
<tr>
<th>Category</th>
<th>Count</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome 1</td>
<td>100</td>
<td>80.5</td>
<td>5.2</td>
</tr>
<tr>
<td>Outcome 2</td>
<td>50</td>
<td>75.0</td>
<td>3.8</td>
</tr>
<tr>
<td>Outcome 3</td>
<td>15</td>
<td>85.5</td>
<td>4.1</td>
</tr>
</tbody>
</table>

Note: Further analysis required for clinical applicability.
### Clinical evidence: egg donation program (RCT)

#### Table 1: Multicentric longitudinal cohort study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Absolute number</th>
<th>Mean (95%CI)</th>
<th>% (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycles</td>
<td>436</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Warmed oocytes</td>
<td>2721</td>
<td>5.62 (5.32-5.93)</td>
<td></td>
</tr>
<tr>
<td>Survived oocytes</td>
<td>2304</td>
<td>4.78 (4.54-5.03)</td>
<td>84.7 (83.3-86.0)</td>
</tr>
<tr>
<td>Inseminated oocytes</td>
<td>2182</td>
<td>4.53 (4.28-4.77)</td>
<td>94.7 (93.7-95.5)</td>
</tr>
<tr>
<td>Fertilized oocytes</td>
<td>1642</td>
<td>3.41 (3.19-3.62)</td>
<td>75.2 (73.4-77.0)</td>
</tr>
<tr>
<td>Top quality embryos</td>
<td>796</td>
<td>1.89 (1.57-2.20)</td>
<td>48.1 (45.7-50.5)</td>
</tr>
<tr>
<td>Embryo transfers</td>
<td>436</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delivery</td>
<td>128</td>
<td>5.4%</td>
<td></td>
</tr>
<tr>
<td>Newborn</td>
<td>147</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 of warmed oocytes; 2 of survived oocytes; 3 of inseminated oocytes; 4 of fertilized oocytes; 5 of cycles; 6 of embryo transfers; 7 of transferred embryos.
Embryo vs oocyte vitrification in the infertile population

The purpose of this work has been to analyze the effects deriving from the change of the Italian law (no embryo cryopreservation vs embryo cryopreservation).

A one-to-one matched case-control study was conducted with good responder patients to evaluate the impact of embryo selection and embryo cryopreservation.

Cumulative outcomes

<table>
<thead>
<tr>
<th>Table 6: Cumulative outcomes</th>
<th>F single</th>
<th>F single</th>
<th>F single</th>
<th>F single</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-vitro cycle (%)</td>
<td>98.8</td>
<td>98.8</td>
<td>98.8</td>
<td>98.8</td>
</tr>
<tr>
<td>Cumulative pregnancy rate (%)</td>
<td>38.8</td>
<td>38.8</td>
<td>38.8</td>
<td>38.8</td>
</tr>
<tr>
<td>Cumulative births (%)</td>
<td>14.7</td>
<td>14.7</td>
<td>14.7</td>
<td>14.7</td>
</tr>
</tbody>
</table>

Perinatal outcomes

Commentary

Obstetric and perinatal outcome in 250 infertile women conceived from vitrified oocytes
As for IVF in general, oocytes and embryos are exposed to some stress when working in vitro that may compromise physiology, gene expression and development.

Vitrification potential risks

- Suboptimal in vitro conditions and extra stress can lead to irreversibly long-term alterations in the characteristics of foetal and postnatal growth and development (Lucilero et al., 2004)

Conclusions

"Compared to the extended life expectancy of modern humans, women face a relatively early loss of fecundity. This was referred to as 'BIOLOGICAL INEQUITY,' a situation from which oocyte cryopreservation may now for the first time help them to escape." Dondorp et al., 2009

- Vitrification is at the moment the most efficient approach for oocyte cryopreservation (as reported by RCT and meta-analysis).
- Vitrification allows at any stage of development:
  - Excellent survival and development ability
  - Consistent and reproducible results
  - Optimal timing of cryopreservation

Is oocyte vitrification an alternative to embryo cryopreservation?

<table>
<thead>
<tr>
<th>Survival</th>
<th>85 – 90%</th>
<th>90 – 95%</th>
<th>85 – 95%</th>
<th>70 – 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implantation</td>
<td>15 – 18%</td>
<td>15 – 20%</td>
<td>20 – 30%</td>
<td>25 – 40%</td>
</tr>
<tr>
<td>Number</td>
<td>10</td>
<td>7</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

"To him who devotes his life to science, nothing can give more happiness than increasing the number of discoveries, but his cup of joy is full when the results of his studies immediately find practical applications." Louis Pasteur
Oocyte banking in an egg-donation programme

Elisabeth Clare Larsen MD PhD
The Fertility Clinic - Rigshospitalet Copenhagen University Hospital
Denmark

Conflict of interest

• I confirm, that I do not have any commercial or financial relationships related to this presentation and its contents

Learning objectives

• To give an overview in the the principles of egg-donation:
  – Definition
  – Indications
  – The procedure (fresh cycle)
• To give a short introduction to oocyte banking:
  – Definition
  – Indications
• To present the latest research in the field of:
  – Oocyte banking in an egg-donation programme
  – Discuss PROs and CONs
Egg-donation: historical background

- First pregnancies reported in 1983 and 1984
- Observation:
  1. Pregnancy rates independent of the age of the recipient
  2. A fertility treatment that overcomes the age-related decline in female fertility
- Today, there is a widespread use of this technique

Egg-donation Definition:

- Fertility treatment where a woman (the donor) donates unfertilized eggs to a couple where the female partner (the recipient) has no functional eggs in the ovaries.

Egg-donation Important:

- The donor needs hormonal stimulation to develop eggs
- The recipient needs estrogen replacement to develop a receptive endometrium
- Well synchronized replacement of high-quality embryos is crucial
- The recipient is pregnant
- The recipient delivers the baby
- Efficient treatment
  - Pregnancy rate – 46.2% per transfer (ESHRE 2007)
  - Delivery rate – 30.2% per transfer (ESHRE 2007)
22 countries – 15,731 treatment cycles with Egg-donation

United States 2009:
1,7697 oocyte donation cycles
12% of all ART cycles that year
Egg-donation

- Indication:
  - Both Ovaries removed
    - Endometriosis
    - Borderline cysts

- Indication:
  - Ovaries removed
  - Turner’s syndrome

- Indication:
  - Ovaries removed
  - Turner’s syndrome
  - Premature menopause
    - < 40 years
Egg-donation

- **Indication:**
  - Ovaries removed
  - Turner’s syndrome
  - Premature menopause
    - < 40 years
  - Anti-neoplastic treatment in childhood and adolescence (ovarian failure)
  - Low ovarian reserve (IVF failure)
  - Possibility in women with genetic diseases where preimplantation genetic diagnosis (PGD) is not a possibility or if the woman refrain from PGD
Egg-donation Procedure (Fresh cycle)

Donor:
- rFSH cd 3-12
- Ovulation induction
- Drum pick up

Recipient:
- E2 cd 2-12
- Progesterone
- Semen sample
- ET

Syncronization – a challenge with pitfalls

- Donor:
  - Normally regular cycles (23-35 days)
  - Complete control
    - contraceptive pill one-two months before donation
- Recipient:
  - Normally hormonal replacement therapy
  - Before oocytedonation
    - Estrogen replacement for up to 50 days
Oocyte banking - definition
Oocyte banking is the procedure by which a woman stores unfertilized oocytes for future fertility use.

Oocyte banking - Indications
- Young women with malignant diseases
  - Potentially sterilizing therapy
- Young women with a low ovarian reserve
  - Ovarian surgery, endometriosis
- Infertile women at risk of developing ovarian hyperstimulation syndrome (OHSS)
- Unavailability of a male gamete on the day of ovum pick-up
- Egg donation
- Social freezing
  - Women who wish to delay motherhood

Oocyte banking - Procedure
- Conventional ovarian stimulation
- Ovum pick up
- Oocytes are denudated
- Oocytes are vitrified
Oocyte banking in an egg-donation programme

Does it work?

YES!!

Case control study from 2011

Conclusion: "Vitrified oocytes preserve the potential to develop into high quality embryos similar to embryos from fresh oocytes."

Table 1: Study group vs Controls

<table>
<thead>
<tr>
<th></th>
<th>Study group</th>
<th>Controls</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oocytes (n)</td>
<td>312</td>
<td>786</td>
<td></td>
</tr>
<tr>
<td>Metaphase II oocytes</td>
<td>283 [90%]</td>
<td>606 [80%]</td>
<td></td>
</tr>
<tr>
<td>Vitrified oocytes</td>
<td>283</td>
<td>191</td>
<td></td>
</tr>
<tr>
<td>Survived oocytes</td>
<td>253 [89.4%]</td>
<td>608 [87%]</td>
<td></td>
</tr>
<tr>
<td>Injected oocytes</td>
<td>251</td>
<td>695</td>
<td></td>
</tr>
<tr>
<td>Fertilized oocytes</td>
<td>191 [76%]</td>
<td>608 [87%]</td>
<td></td>
</tr>
<tr>
<td>Good embryos day 2</td>
<td>90.8%</td>
<td>84.3%</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS = Not significant
Table 2

<table>
<thead>
<tr>
<th>Study group</th>
<th>Controls</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fertilized oocytes (n)</td>
<td>191</td>
<td>608</td>
</tr>
<tr>
<td>Morula day 4 (n)</td>
<td>121 (63.4%)</td>
<td>361 (59.6%)</td>
</tr>
<tr>
<td>Blastocysts (n)</td>
<td>79 (41.3%)</td>
<td>276 (45.3%)</td>
</tr>
<tr>
<td>Good blastocysts (%)</td>
<td>75 (0.10)</td>
<td>77.4 (0.14)</td>
</tr>
<tr>
<td>Early blastocysts (%)</td>
<td>25</td>
<td>18.9</td>
</tr>
<tr>
<td>Full blastocysts (%)</td>
<td>50.8</td>
<td>23.3</td>
</tr>
<tr>
<td>Expanded (%)</td>
<td>35.5 (n=28)</td>
<td>52.6 (n=145)</td>
</tr>
<tr>
<td>Hatched (%)</td>
<td>2.6</td>
<td>1.5</td>
</tr>
</tbody>
</table>

NS = Not significant

• To summarize
• 283 vitrified oocytes
• 253 or 89% survived vitrification
• Out of 191 fertilized oocytes (ICSI) 173 developed into good quality embryos (day 2)
• Out of 191 fertilized oocytes 79 developed into blastocysts eligible for transfer

*Oocyte cryopreservation for donor egg banking*

**Review from 2011**

Conclusion: "The benefits of a donor egg bank make it likely that this approach becomes the future standard of care."

Page 52 of 100
### Oocyte cryopreservation for donor egg banking

Asa Coker*, Jeni Rameau*, Ching-Chao Chang†, David Peter-Magg ‡

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Donation cycles (n)</td>
<td>1051</td>
</tr>
<tr>
<td>Recipient cycles (n)</td>
<td>919</td>
</tr>
<tr>
<td>Age recipient (years)</td>
<td>41.2 (mean)</td>
</tr>
<tr>
<td>Total oocytes warmed (pr recipient)</td>
<td>12786 oocytes (12.9)</td>
</tr>
<tr>
<td>Total oocytes for ICSI (pr recipient)</td>
<td>11949 oocytes (11.4)</td>
</tr>
<tr>
<td>Fertilization rate (two PN)</td>
<td>8920 (74.7%)</td>
</tr>
<tr>
<td>High quality embryos on day 3 (n)</td>
<td>5366 (44.9%)</td>
</tr>
<tr>
<td>Embryos extended culture (n)</td>
<td>3568</td>
</tr>
<tr>
<td>High quality embryos on day 5</td>
<td>1427 (40%)</td>
</tr>
<tr>
<td>Implantation rate (fresh cycle)</td>
<td>655/1655 (39.6%)</td>
</tr>
<tr>
<td>Embryos cryopreserved</td>
<td>1915</td>
</tr>
<tr>
<td>Clinical pregnancies (n) per transfer (%)</td>
<td>502 (55.4%)</td>
</tr>
</tbody>
</table>

5/18/2013  ESHRE 2013 PCC1
Oocyte cryopreservation for donor egg banking

Aue Cacho*, June Kamara*, Chong Chau Chang*, Cishi Panegyri*^*

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<tr>
<td>Implantation rate</td>
<td>655/1655 39.6%</td>
</tr>
<tr>
<td>Clinical pregnancies</td>
<td>502 (55.4%)</td>
</tr>
</tbody>
</table>

To summarize:
- 12786 Donor eggs
- 502 Clinical pregnancies
- 343 Babies (180 girls and 163 boys)
  > 10 more babies from subsequent embryo cryotransfer

Oocyte banking in an egg-donation programme - CONs

- Cost:
  – Expensive in laboratory utilities
  – Time consuming in the laboratory
- Frozen cycle?
Oocyte banking in an egg-donation programme - CONs

- Cost:
  - Expensive in laboratory utilities
  - Time consuming in the laboratory
- Frozen cycle? – good results with vitrified oocytes!

CA. Outcome of cryotransfer of embryos developed from vitrified oocytes: double vitrification has no impact on delivery rates. Fertility and Sterility, 02/28/2013

<table>
<thead>
<tr>
<th>Group 1 (vitrified oocytes)</th>
<th>Group 2 (fresh oocytes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>471 warming cycles</td>
<td>2629 warming cycles</td>
</tr>
<tr>
<td>796 embryos thawed</td>
<td>4394 embryos thawed</td>
</tr>
<tr>
<td>Survival rate 97.2%</td>
<td>Survival rate 95.7%</td>
</tr>
<tr>
<td>Delivery rate 99.8%</td>
<td>Delivery rate per cycle:</td>
</tr>
<tr>
<td></td>
<td>30.9%</td>
</tr>
</tbody>
</table>

Survival rate 97.2%
Cobo A. Outcome of cryotransfer of embryos developed from vitrified oocytes: double vitrification has no impact on delivery rates. Fertility and Sterility, 02/28/2013

Group 1 (vitrified oocytes) • Delivery rate per cycle: 33.8%

Group 2 (fresh oocytes) • Delivery rate per cycle: 30.9%

Controlled for confounding factors:
1. Egg-donation or autologous cycles,
2. Day-3 or blastocyst transfer
3. Natural or hormonal replacement cycle for ET
4. Single or double embryo transfer
5. Previous cycles
6. Number of oocytes
7. Doses of gonadotropins
8. Estradiol levels on the day of hCG

Double vitrification has no impact on delivery rates

Oocyte banking in an egg-donation programme – PROs:
- Firstly:
- A large donor pool
- Recipients are guaranteed 5 to 7 mature eggs per cycle
- Low risk of cycle cancellation
  – Less than 3%
Oocyte banking in an egg-donation programme – PROs:

•  Secondly:
•  Synchronization not required!!
•  Donor eggs used when endometrial preparation in recipient is completed
  – No prolonged use of estrogen replacement with the risk of cancellation (breakthrough bleeding)
•  No canceled cycles due to donors who fail pre-screening or has an unexpected low response
•  Permission of a more accurate screening of infectious diseases
  – Oocytes in “quarantine” for 6 months until confirmation of serology of the donor

Indeed more PROs than CONs

Egg banking in the United States: current status of commercially available cryopreserved oocytes

Indeed more PROs than CONs
Egg banking in the United States: current status of commercially

Conclusion: Frozen donor eggs are currently widely available
in the United States

Important figures

- Seven commercial egg banks in the United States
  - All 7 answered the survey
- Existed for 2 years (median)
  - Range 1-8 years
- Currently 21.5 donors (median)
  - Range 6-100 donors
- Currently 120 available oocytes (median)
  - Range 20-1000 oocytes
- Recommended number of eggs was 6 per cycle
  - Range 4-7

<table>
<thead>
<tr>
<th>Table 1: Oocytes donated by each of the seven identified commercial egg banks in the United States.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg bank</td>
</tr>
<tr>
<td>CRL</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
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<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>7</td>
</tr>
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<td></td>
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</tbody>
</table>
Take home messages

- Egg donation has high and comparable pregnancy and delivery rates when using fresh and vitrified oocytes
- Double vitrification does not affect delivery rates
- In an egg donation programme oocyte banking has more PROs than CONs
- Vitrification of donor oocytes is the solution for the logistic problems commonly occurring in an egg donation programme
- Oocyte banking is a promising new phenomenon

Thank you

Elisabeth Clare Larsen MD PhD
The Fertility Clinic
Juliane Marie Centre
Rigshospitalet
Denmark

References

- Cobo et al. Outcome of cryotransfer of embryos developed from vitrified oocytes: double vitrification has no impact on delivery rates. Fertil and Steril 02/28/2013 Clinical Article.
Learning Objectives

Appreciate the current status of oocyte cryopreservation as the technology becomes increasingly applied to females with the need and/or desire

Indications for Oocyte Cryopreservation

1. Medical
   - Newly-diagnosed malignancy requiring gonadotoxic therapy
   - Non-cancer medical conditions
     • Sickle cell, Systemic lupus erythematosus, Scleroderma, BRCA gene mutation carrier
   - IVF indications
     • Lack of sperm day of retrieval
     • Risk for ovarian hyperstimulation syndrome

2. Oocyte donation - “Donor Banks”

3. Personal reasons for deferring parenthood

4. Emergencies
**2006 ASCO Guideline Summary**

As part of informed consent prior to therapy, oncologists should address the possibility of infertility with patients as early in treatment planning as possible.

FP is an important, if not necessary, consideration when planning cancer treatment in reproductive-age patients.

*Lee SJ, Schover LR, et al., J Clin Oncol 2006*
Bone Marrow Transplantation
Associated with Ovarian Failure

- Bone Marrow Ablation/Transplantation
  - Myelosuppressive chemotherapy (high-dose cyclophosphamide + busulfan or thiotepa) and irradiation

Ovarian Failure following BMT
Sanders, 1996 99%
Teinturier, 1998 72%
Thibaud, 1998 80%
Meir, 1999 79%
Grigg, 2000 100%

2. Donor Egg Banking
Demand at an all-time high

USA: 15,000 DE transfers/year (SART.org 2009)
3. Personal Indications

4. Emergencies

Hurricane Sandy
October 2012
DIMINISHING OVARIAN RESERVE

20 weeks gestation: 6-7 x 10^6 oocytes
No further germ cell proliferation
Progressive atresia begins

Birth: 1-2 x 10^7 oocytes
Oocytes arrested at prophase I, as primordial or primary oocytes

Puberty: 300,000 (15%) oocytes
Monthly cohort of follicles undergo growth and development
use "ovulates" others become atretic

Age 40: 200,000 (~12%) oocytes
Age 45: 60,000 (~3%) oocytes
accelerated atresia

Coincident is a ↓ in quality of oocytes

WOMEN ARE WAITING TO HAVE CHILDREN

U.S. Census Data

Given the choice, both men and women prefer Reproductive Autonomy

Not only are people having children later, they’re having less children. WHY?

Professional/life aspirations, responsibility, economics, readily available birth control and less ‘need’ for offspring in the early reproductive years

Hutterites:
Average # live births per woman:
1950s → 9 - 10
1980s → 5

Why?
Technology
Advanced farm equipment
Oocyte Cryopreservation History

- First human pregnancy was reported in 1986
- Early results disappointing
  - Low oocyte survival, fertilization and pregnancy rates
- Why oocytes difficult to freeze –
  - Large cell size (100 micrometers)
  - Ice crystal formation
    - Aqueous: High water content (80%)
    - Chromosomal arrangement (spindle)

Oocyte Cryopreservation Breakthroughs

- Fine-tuning dehydration protocols through modifications in cryoprotectant combinations, concentrations and exposure times
- Fertilization by Intracytoplasmic Sperm Injection (ICSI) - 1995
  - Circumvents zona pellucida hardening that may occur during freezing process
- Development of novel “cryotools”

Human Oocyte Cryopreservation Worldwide

<table>
<thead>
<tr>
<th>Literature-Reported Live Births</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Births</td>
<td>2000</td>
</tr>
<tr>
<td>Slow Cooling (n = 308)</td>
<td>2015</td>
</tr>
<tr>
<td>Vitrification (n = 200)</td>
<td>2015</td>
</tr>
<tr>
<td>Both (n = 12)</td>
<td>2015</td>
</tr>
</tbody>
</table>

Barnes, Spero, Inc. Report Revised April 2000:19-21
Comprehensive review of oocyte cryopreservation safety and success as of 2007

Experimental Designation

Cumulative Oocyte Preservation Outcome Data

No increase in birth anomalies

Oocyte Cryopreservation
Survey of USA IVF centers

- 442 centers contacted:
  282 (64%) responded over 49 states
- 51% of programs currently offer oocyte cryopreservation
- 337 live births from 857 thaw cycles: 39.3% live birth rate
  ~Similar to embryo thawing success

Mature oocyte cryopreservation: a guideline

Two Major Cryo Methods

NYU Fertility Center Thaw Data
Oocytes From Women < Age 40
Slow-Cooled vs. Vitrification
Supporting Data for Oocyte Banking
Donor Oocyte Cycles
Randomized Controlled Trial - Vitrified vs. Fresh

<table>
<thead>
<tr>
<th></th>
<th>Vitrified Oocytes n = 295</th>
<th>Fresh Oocytes n = 289</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age of egg donor (y)</td>
<td>26.7</td>
<td>26.5</td>
</tr>
<tr>
<td>Estradiol day hCG (pg/ml)</td>
<td>2879</td>
<td>2992</td>
</tr>
<tr>
<td>Mean no. oocytes</td>
<td>10.3</td>
<td>11.2</td>
</tr>
<tr>
<td>Fertilization %</td>
<td>74.2</td>
<td>73.3</td>
</tr>
<tr>
<td>Mean no. embryos transferred</td>
<td>1.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Implantation rate %</td>
<td>29.9</td>
<td>40.0</td>
</tr>
<tr>
<td>Clinical pregnancy rate/transfer %</td>
<td>52.4</td>
<td>53.6</td>
</tr>
</tbody>
</table>

Oocyte Cryopreservation
Donor Oocyte – Fresh vs. Vit
77 transfers

<table>
<thead>
<tr>
<th></th>
<th>Fresh</th>
<th>Vit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fertilization %</td>
<td>74.2</td>
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</tr>
</tbody>
</table>

Semen analysis of donors

<table>
<thead>
<tr>
<th></th>
<th>Fresh</th>
<th>Vit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motility %</td>
<td>60</td>
<td>55</td>
</tr>
<tr>
<td>Total sperm count</td>
<td>56</td>
<td>50</td>
</tr>
<tr>
<td>Motile sperm count</td>
<td>24</td>
<td>20</td>
</tr>
</tbody>
</table>

Embryo development of fresh “versus” vitrified metaphase II oocytes after ICSI: a prospective randomized sibling-oocyte study

<table>
<thead>
<tr>
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</table>

OC can offer comparable outcomes to fresh ICSI even when using a restricted # of oocytes.
NYU Fertility Center
Oocyte Cryopreservation Data
2004 - 2013

- 60% Deferred Reproduction
- 40% Medical
- 7 Oocytes + 6 Embryos Thaws
- DR patients come back sooner

NYU Fertility Center Non-Cancer Thaw Data
Oocytes From Women ≤Age 42
n = 70 cycles: 21 donor + 49 autologous

<table>
<thead>
<tr>
<th></th>
<th>Donor 21-31 y (n = 21)</th>
<th>Autologous 25-34 y (n = 17)</th>
<th>Autologous 35-39 y (n = 18)</th>
<th>Autologous 40-42 y (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y)</td>
<td>29</td>
<td>32</td>
<td>38</td>
<td>41</td>
</tr>
<tr>
<td>No. MII thawed</td>
<td>11</td>
<td>16</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>No. transferred</td>
<td>2.1</td>
<td>2.1</td>
<td>2.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Pregnant n (%)</td>
<td>17 (81%)</td>
<td>10 (59%)</td>
<td>7 (39%)</td>
<td>3 (21%)</td>
</tr>
<tr>
<td>Spont Abortion</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ongoing/Delivered</td>
<td>14 (70%)</td>
<td>9 (53%)</td>
<td>6 (33%)</td>
<td>2 (14%)</td>
</tr>
</tbody>
</table>

Mean: 2.1 embryos each cycle and ≤1 embryo/thaw cycle

- Excludes PGD/PGS cycles and ≥43 y oocytes
- *1 baby from refrozen embryos

Ongoing/LBR: 31/70 = 44% (Autologous: 17/49 = 35%)
25 women have delivered 32 liveborn infants + 6 ongoing pregnancies

No. of OC cycles performed for DR at NYUFC per year

![Graph showing the number of OC cycles performed for DR at NYUFC per year](image)
After documenting success using OC techniques, we began offering OC as a measure for cancer patients. Patients offered Oocyte (OC) and/or Zygote Cryopreservation (ZC). Evaluation includes 166 female cancer patients referred for FP from April 2005 to October 2012. 152 pursued treatment (mean age 31 y):

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Partnered (%)</th>
<th>Not Partnered (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GYN</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>OC – Cancer</td>
<td>47</td>
<td>53</td>
</tr>
<tr>
<td>OC with thaw – Non-Cancer</td>
<td>47</td>
<td>53</td>
</tr>
</tbody>
</table>

Demographics and Cycle Outcomes:

- Patient age (y): 31 ±1
- Days from REI consult to retrieval when treatment deemed urgent: 17 (8 – 30)
- Days ovarian stimulation: 10 (5 – 12)
- E2 day of ovulation trigger (pg/ml): 1785 (319 – 6881)
- No. oocytes retrieved (n = 2,878): 18 (0* – 75)
- No. mature (MII) oocytes (n = 2,195): 14 (0* – 53)

Breast (n = 54)
Hematol (n = 30)
GYN (n = 52)
OC – Cancer (n = 50)
OC with thaw – Non-Cancer (n = 32)

Werner et al. JARG 2010;27:613

NYUFC Data – By Cancer Type
2005 – 2012

Age (y):

- Breast
- GYN
- Heme

Partnered:

- Breast
- GYN
- Heme

E2 @ Trigger (pg/ml):

- Breast
- GYN
- Heme

MII Oocytes Retrieved:

- Breast
- GYN
- Heme

Noyes et al. Unpublished data
Study group (n=51) | Control group (n=50) | P-value
--- | --- | ---
# Stimulation Days | 13 ± 3 | 11 ± 4 | 0.02*  
Peak E2 (pg/mL) | 2114 ± 1408 | 2161 ± 1075 | 0.8  
# Oocytes | 20 ± 13 | 24 ± 14 | 0.1  
% MII Oocytes | 82 | 86 | 0.8

Don’t dose up unless prior chemotherapy

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No.</th>
<th>Age (y)</th>
<th>Eggs Frozen</th>
<th>Eggs Thawed</th>
<th>Oocytes</th>
<th># 2PN Frozen</th>
<th># 2PN Transferred</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical Cancer</td>
<td>28</td>
<td>12</td>
<td>14</td>
<td>2</td>
<td>Twins</td>
<td>Ongoing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS</td>
<td>29</td>
<td>88</td>
<td>3</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus Sarcoma</td>
<td>31</td>
<td>66</td>
<td>2</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>33</td>
<td>12</td>
<td>12</td>
<td>2</td>
<td>Spont Ab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>40.5</td>
<td>14</td>
<td>8</td>
<td>6</td>
<td>4</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>34</td>
<td>83</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>39</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical Adenocarcinoma</td>
<td>29</td>
<td>15</td>
<td>14</td>
<td>2</td>
<td>1</td>
<td>Singleton</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ewing’s Sarcoma</td>
<td>29</td>
<td>12</td>
<td>11</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>Singleton</td>
</tr>
<tr>
<td>Ovary</td>
<td>30</td>
<td>43</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical Adenocarcinoma</td>
<td>29</td>
<td>12</td>
<td>11</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>Negative</td>
</tr>
<tr>
<td>Breast</td>
<td>32</td>
<td>22</td>
<td>25</td>
<td>9</td>
<td>7</td>
<td>2</td>
<td>Spont Ab</td>
<td></td>
</tr>
</tbody>
</table>

Means: 32.0 y; 129.0 oocytes; 41.0 zygotes
6/12 (50%) successful; 1 twice

GnRH Ag Trigger

No OHSS when use GnRH Ag Trigger

Individual Patient Response

Medical Thaw Cycles
12 patients completed 35 cycles: 12 zygotes and 7 oocyte thaws
Hurricane Sandy

- 19 cycles performed elsewhere
- 9 oocyte cryopreservation cycles in lieu of IVF
- Mean age: 35±2 y
- 60% ongoing pregnancy rate

Conclusions

- Oocyte cryopreservation is a reasonable FP option being embraced in the USA for expanding list of indications
- Ideally, oocyte cryopreservation offers the broadest clinical application, has achieved the greatest strides in the last decade and now can result in reasonable pregnancy outcomes in appropriately selected candidates
- Prior to proceeding with any FP measure, interested individuals require thoughtful counseling and should be provided realistic statistics and options related to their reproductive future
- Disposition issues must be considered and discussed, especially in the setting of cancer
  - Ethics, Her rights
- Cost/Insurance coverage
  - Removal of an “experimental” label should improve insurance coverage for some patients/indications
THANK YOU
nicole.noyes@nyumc.org
Counseling of women opting for oocyte cryopreservation for prevention of age related fertility loss or ‘Social Freezing’

Prof. Dr. Julie Nekkebroeck
ESHRE 07/07/2013 - London

Learning Objectives

- Have more insight in the profile of women applying for oocyte vitrification for non-medical reasons
- Learn about why social freezers need counseling
- Learn about how to counsel social freezers

Overview of the presentation

- What is social freezing?
- What is counseling?
- Are social freezers in need of counseling?
- Guidelines for counseling
- How do we counsel at the CMG UBrussel?
- Overview of the population sample
- Conclusions
- References
What is social freezing?

- Women will deliberately postpone motherhood
- Mostly career women
- No guarantee on childbearing hence, false hope
- A stress-inducing high technological fertility treatment without having an actual fertility problem
- Safety of the ART techniques for later fertility and the impact on child development

What about women’s benefits and reproductive autonomy and equal opportunities for men and women?

What is counseling?

**Definition and aims of counseling**

- Support, guidance and advice rather than change
- Explore, understand and resolve infertility (treatment) issues
- Clarify ways of dealing with the problem
- Consider the needs of the patient and other affected persons
- Different functions and/or goals

---

**Counseling within infertility (Strauss, B., Boivin, J. 2002)**
Social freezers in need of counseling?

1. High Distress levels

2. Third party reproduction
   - To be assisted with oocyte vitrification

3. Fertility service because of social circumstances
   - Single motherhood
   - Lesbian motherhood
   - Oocyte vitrification

"Cryopreservation for social and not medical reasons means that the freezing institution is dealing with a customer and not an infertile patient. The management of customer expectations is radically different from infertile patients as there is 'nothing wrong with them'; they are simply using a service." (BioNews 2009).

Guidelines for counseling in infertility: outline version (Boivin, J. et al. 2001)

Social freezers in need of counseling?

<table>
<thead>
<tr>
<th>Personal Factors</th>
<th>Social Freezer?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-existing psychopathology</td>
<td>YES</td>
</tr>
<tr>
<td>Primary infertility</td>
<td>NO</td>
</tr>
<tr>
<td>Being a woman</td>
<td>YES</td>
</tr>
<tr>
<td>Parenting = central goal</td>
<td>YES</td>
</tr>
<tr>
<td>Avoidance coping strategy</td>
<td>YES</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Situational Factors</th>
<th>Social Freezer?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor partner relationships</td>
<td>YES</td>
</tr>
<tr>
<td>Isolated social network</td>
<td>NO</td>
</tr>
<tr>
<td>Frequent reminders of infertility</td>
<td>NA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment Factors</th>
<th>Social Freezer?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Side effects of medication</td>
<td>YES</td>
</tr>
<tr>
<td>Miscarriages</td>
<td>NO</td>
</tr>
<tr>
<td>Prior treatment failure</td>
<td>NO</td>
</tr>
</tbody>
</table>

YES, they are!!

Because:

- Use of a fertility service for non-medical reasons
  - Offer implication and informed decision-making counseling
- (High) Distress might be experienced
  - Offer support counseling / crisis counseling
Guidelines for Counseling

**Do’s**

Discuss:
- Fertility preservation for what it is
- Best chance of having a child
- Small percentage of women actually using the oocytes
- Alternatives
- Nature, risks, and limitations of the procedure, the storage conditions, the time frame for use, the costs, the use and fate of the left-over oocytes
- Number of oocytes required for successful reproduction
- The long-term safety of the oocytes

**Dont’s**

- Raise false hopes!
- Present this option as a warrant for successful future reproduction (Harwood, 2009)
- Recommend oocyte cryopreservation for women > 38 years

---

**Procedure at the CRM UZBrussel**

- Medical assessment and information sharing by the doctor
- Semi-structured Interview by the psychologist
- Multidisciplinary advice; binding and only in specific situations
- Discussion of the results from the blood samples, ultrasounds etc. by the doctor
- Explanation of the treatment, informed consents, financial aspects and planning by the counselor

---

**Procedure: Responsibilities of the psychologist**

- Perform a screening interview
- Formulate an advice concerning treatment  
  - Gatekeeper function
- In case of contra-indication(s): presentation of the case at the Bioethics committee (CRG/CMG)
- Offer psychological advice or support prior, during or after treatment on request of the doctor or the patient
- Re-evaluation when the candidate wants to recuperate her cryopreserved oocytes!!
Procedure: Screening interview

- Socio-demographics: age, nationality, profession, education
- Family background: parents, siblings, quality of the family relations
- Relationships: relational status, number, duration and quality of relations in the past, desire partner vs. desire for a child, actively searching for a partner
- Desire for a child: presence of the desire, reason for childlessness
- Discovery of the possibility to vitrify oocytes
- Motives to opt for this treatment and/or alternatives
- Openness and received support
- The treatment: ethical/moral aspects, (de)advantages, number, financial aspects
- Use of the vitrified oocytes: age, pathways to conception, destination of left-over oocytes

Procedure: Contra-indications

- Intake interview did not take place before the 40th birthday
- Hormonal problems – Fertility status?
- Psychiatric problems confirmed by a psychiatric diagnosis and/or a team of specialists and/or for which a therapy was necessary (medication/psychotherapy)
- Dependency problems (alcohol, drugs, psycho pharmaceutical drugs)
- Financial problems
- Mental retardation
- Physical impairment (motor, visual and/or audibility) and/or suffering from a chronic degenerative and/or genetic disorder
- Or a combination of the above

Advice from the Bio-ethics committee of the Centre for Reproductive Medicine and the Centre for Medical Genetics

Overview of our population sample

225 candidates between July 2009 - September 2012

225 candidates between July 2009 - September 2012

115 treated

69 Potential starters

19 Refusals

13 undecided

18 other reasons

Av. N° OPU: 1.78 (±1.065)
Socio-demographics

Age at intake 37.02 (±2.6; 24-43y)

<table>
<thead>
<tr>
<th>Educational level</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>University degree</td>
<td>64.1%</td>
</tr>
<tr>
<td>Degree</td>
<td>31.8%</td>
</tr>
<tr>
<td>School matriculation</td>
<td>4.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>% Employment</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full time</td>
<td>80.5%</td>
</tr>
<tr>
<td>Unemployed</td>
<td>9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Language</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dutch</td>
<td>72%</td>
</tr>
<tr>
<td>French</td>
<td>24.4%</td>
</tr>
<tr>
<td>English</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nationality</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dutch</td>
<td>52%</td>
</tr>
<tr>
<td>Belgian</td>
<td>24.9%</td>
</tr>
<tr>
<td>EU/Other</td>
<td>23.1%</td>
</tr>
</tbody>
</table>

Relationships and mental health

<table>
<thead>
<tr>
<th>Relational status</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>71.6%</td>
</tr>
<tr>
<td>New relationship</td>
<td>12.9%</td>
</tr>
<tr>
<td>Ongoing relationship</td>
<td>12.9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relationships in the past</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>99.2%</td>
</tr>
<tr>
<td>Not applicable</td>
<td>26%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Latest break-up</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1 year ago</td>
<td>36.5%</td>
</tr>
<tr>
<td>1 year or more</td>
<td>32.5%</td>
</tr>
<tr>
<td>Not applicable</td>
<td>26%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Therapy</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>21.3%</td>
</tr>
<tr>
<td>Medication</td>
<td>7.1%</td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>8%</td>
</tr>
<tr>
<td>Combination</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Children</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>2.2%</td>
</tr>
<tr>
<td>No</td>
<td>97.8%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abortion(s)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>13.3%</td>
</tr>
<tr>
<td>No</td>
<td>86.7%</td>
</tr>
</tbody>
</table>

Child desire

<table>
<thead>
<tr>
<th>Since when?</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never really outspoken</td>
<td>15.6%</td>
</tr>
<tr>
<td>Recent 0-5 years</td>
<td>37.8%</td>
</tr>
<tr>
<td>Always</td>
<td>44%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Versus desire for a partner</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mostly desire for a partner</td>
<td>35.1%</td>
</tr>
<tr>
<td>Mostly desire for a child</td>
<td>8.4%</td>
</tr>
<tr>
<td>Both are connected</td>
<td>32%</td>
</tr>
<tr>
<td>None of both/NA</td>
<td>23%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Why not fulfilled?</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No right partner</td>
<td>57.8%</td>
</tr>
<tr>
<td>Priority to career</td>
<td>4%</td>
</tr>
<tr>
<td>Undecided about having children</td>
<td>4.4%</td>
</tr>
<tr>
<td>Partner has no child desire</td>
<td>4%</td>
</tr>
<tr>
<td>Late bloomers</td>
<td>8.4%</td>
</tr>
<tr>
<td>Combination</td>
<td>14.3%</td>
</tr>
</tbody>
</table>
Discovery and Motives

- Discovery:
  - N°1 Media (32.4%)
  - N°2 Friends, colleagues, relatives (19.6%)
  - N°3 Internet (15.6%)
  - N°4 Gynecologist, general practitioner (7.1%)

- Main reasons:
  - Assurance against future age-related infertility
  - Buying more time to find a suitable partner

Alternatives

- Search for a suitable partner = only valuable alternative
- 60% actively searches for a partner by visiting dating sites, addressing their social network, ...

Openness and support from the social network

<table>
<thead>
<tr>
<th>Open?</th>
<th>Yes</th>
<th>97.3%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Informed?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friends</td>
<td>84%</td>
<td></td>
</tr>
<tr>
<td>Parents</td>
<td>52.9%</td>
<td></td>
</tr>
<tr>
<td>Siblings</td>
<td>41.8%</td>
<td></td>
</tr>
<tr>
<td>Partners</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Colleagues</td>
<td>16.9%</td>
<td></td>
</tr>
<tr>
<td>Reactions?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>78.7%</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>17.3%</td>
<td></td>
</tr>
<tr>
<td>Support during treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>89.8%</td>
<td></td>
</tr>
<tr>
<td>Accompanied to hospital + financial support</td>
<td>75.1%</td>
<td></td>
</tr>
<tr>
<td>14.7%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Attitudes and concerns

- No moral, religious (99.6%) or ethical objections (94.2%)
- No concerns about:
  - Undergoing a fertility treatment while being considered fertile (94.7%)
  - Lack of information on the development and health of the children (94.8%)
- Other disadvantages:
  - Fears, stigmatization, gynecological examination, switched oocytes, child-development

Treatment aspects

- 71.4% can afford different treatment cycles on their own
- 26.8% can afford one treatment cycle
- Repeat the treatment 2.11 (±0.64) times depending on:
  - How the first attempt was experienced
  - Number of oocytes retrieved the first time

Use of the vitrified oocytes

- In 79.6% of the cases, when having met the right partner:
  1. Natural conception
  2. IVF with fresh material
  3. Use the vitrified oocytes
- No longer in need of the vitrified oocytes:
  - N°1: Donate for scientific research (33.3%)
  - N°2: Destruction (14.6%)
  - N°3: Known donation (9.1%)
  - N°4: Anonymous donation (6.8%)
  - No idea (25.6%) – Absolutely no destruction (6.8%)
Conclusions: Preliminary profile

- Highly educated single women of an older reproductive age
- Struggling with relationships but having a strong desire for a partner
- Pivotal events
- Simultaneously actively engaging in finding a partner

Advantages
- Aware of the risks and limitations of the treatment
- Precious goods

Conclusions: Counseling

- Women applying for oocyte vitrification for non-medical reasons are to be counseled
- Implication and informed decision-making counseling
- Non-directive with respect for the reproductive autonomy
- Support counseling in case of emotional distress
- More research is needed in order to refine counseling:
  - Follow-up of the vitrification experience
  - Online survey addressing: attitudes towards work, experiences in close relationships, personality features

References

Thank you!

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Thank you!
Ethical issues of Social oocyte freezing
Françoise Shenfield, UCLH, London, member Ethics and Law TF

Disclaimer
The speaker has nothing to disclose

Learning objectives

• To understand what are the ethical issues raised by social oocyte cryopreservation (freezing): SOC
• To be able to analyse them in a systematic manner, whether general or specific
• To be able to question the objections to social freezing (convenience) and argue “pros and cons” (dialectics)
• To understand the legal/demographic and sociological context for access to ART (in Europe), and its application to social freezing
Back to basics: bioethics, and how?

• "Philosophy is not a doctrine, but an activity with the aim to logically clarify one’s thinking" Wittgenstein

Ethics (branch of philosophy): logical analysis of our moral dilemmas

Why? Because we are "citizens in the city" (not merely paramedical, medical, scientists, …)

• Ethics challenges our beliefs and "a priori" positions in a logical fashion; bioethics applies to science and medicine

• Tools (short guide): (3 to) four principles: respect of autonomy; bene v non maleficence; justice

The tools applied to ART and SOC

• The (3 to) 4 principles Beauchamp and Childress

• Autonomy (respect of): women (like men) are autonomous v society/ a profession decides what is good for them ("paternalism"); but the "career woman" may not "choose" to postpone maternity

• Beneficience/Non maleficence: 1 (or 2) patient(s) + future offspring" in ART

• Justice: access via a state funding system; only privately (? equity): or in an insurance system; is there an alternative? (egg donation)

"welfare of the child, in our specialty"

SOC: useful, needed, necessary? (the facts)

• There is a ‘demographic age shift toward later conception (which) results in an increased age in the subfertile population and…

• an increased demand for medical care” (de Graaff, Land, Kessels and Evers, Fort and Ster, 95, 1, January 2011: 61-66)

• Access varies between (European/ worldwide) countries: legal and financial issues (political); this includes age (UK v France)

• Justice: equity of access, limitless access (justice and equity), or age limits (added to other limits already in place)?

• ovarian reserve decrease with female age v male fertility

• There is increased Cross Border Reproductive Care (CBRC), mostly for egg donation
CBRC in 6 European countries: treatment distribution (FS et al, 2010)

- Legal reasons were predominant for Italian patients (70.6%), and the German (80.2%), French (64.9%), and Norwegian (71.6%)
- Access was more often noted in UK patients (34.0%) than in the other countries, and quality was an important factor in most of the countries
- Treatments: 22.2% of patients were seeking IUI only, 73.0% sought ART only, and 4.9% both. Majority of IUI for French (53.3%) and Swedish (62.3%) patients, and a majority of ART for most other countries.
- Gametes and embryo donation, 18.3% of patients were looking for semen donation, 22.8% for OD and 3.4% for ED


- 6 ≤ 34%
- 35 - 39: 35%
- 40 - 44: 30%
- ≥45: 10%

Tenfold rise in fertility treatment for over-40s

- Study shows that there has been a tenfold rise in fertility treatment for women over 40 years old.
- Many couples are choosing to delay having children until they reach their 40s, leading to increased demand for fertility treatments.
- Surrogacy and egg donation are becoming more common as alternatives.
- The rise in fertility treatments for over-40s is a significant trend in modern reproductive medicine.
Scientific background

- Scientific background (discussed today):
  - 1. radical change of technical efficiency since vitrification, non inferior to fresh oocyte in OD programme (Cobo et al 2010); ASRM (2013): not "research" anymore
  - 2. “Unexplained” infertility: more and more “older women, or prejudiced ovarian reserve”
  - 3. less “scientifically”: much web information, not so much at school or university

Objections to SOC (a feminist pragmatic approach)

- Against nature? our daily (scientific) work indeed
- Increased medicalisation of reproduction and the myth of the "selfish career woman": the devil and the deep blue sea: the medical (preserving) model accepted for ca patients, decried for healthy patients. but... knowing one’s reproductive ability will decrease affects... "a person most central life project(s)" and is essential part of wellbeing for many
- Too many > 50 pregnant? (maleficence+ for woman and future child): make the news headlines but a rare event
- In practice, should there be limits to this new reproductive autonomy?

Note: HFEA data - refers to licensed treatments between April 2002 and March 2003
Limits or limitless autonomy?

- Empowering women by informed decision making: the key to autonomy; (potential for) success rates declining with age, number of oocytes needed for 1 pregnancy (from 20-25 vitrified if 4-5% live birth rate per vitrified oocyte; to around 10 if success rate is around 15%. How do you define success?)

- Age limits:
  1. for cryo: honesty in information (no distorted advertising), with age related expectations of number oocytes and number cycles needed as well as costs, safety (non male)
  2. for use: dangers of maternity >50

Mommy's too old

Doing good v less harm (including Welfare Child)

- Beneficence: “emancipation written in stone” (Homburg et al) v “appeal to the limits of medicine” (see contraception, sterilisation); the woman might have remained childless if no SOC

- Non maleficence: how much burden (depends on age and number of cycles necessary); should we stop offering at 35?: need for proper independent evidence based counselling

- Welfare of the child and age of the mother/parents: risk of pregnancy > 50 (use same limits as egg donation); at least one parent able to fulfill parental role till child becomes adult (Ethics and law TF)
Justice and societal implications

- **Who will pay?** Fear that natural reproduction will be replaced by ART and cost to society…. but ART may be more cost effective with younger eggs in older women (Mertens and Pennings 2012)
- **Coverage:** the state, the woman, insurance, fairness and postponed conditional reimbursement
- Left over oocytes may be used for research and donation: use the HFEA model at time of cryopreservation (“if I die or become mentally incapacitated…”): prior consent
- **From OC to OD will rekindle several (ethical) questions:** 1. gametes anonymity France v UK for instance;
  2. compensation (disproportionate?, egg sharing, freeze and share agreement

Other (ethical) advantages

- **The status of the embryo v status of gametes:** 30 years of debate: cases like the Evans case avoided?
- **Transmission of maternal genetic input v egg donation:** the Evans case; also « younger eggs » used at later age (less genetic anomalies)
- Easier management of OD cycle

Other (legal) advantages S.H. v Austria

- **(egg donation) subsidiarity:** the ECIHR held that the individual member states of the Council of Europe should themselves decide whether, how, and when to allow citizens to use reproductive technology
- Austria prohibits egg donation altogether and sperm donation for IVF because it favours genetic ties in parent-child relationships and wishes to protect women who might be exploited by egg donation. Austria does not object to sperm donation for artificial insemination because it is a well-known and not particularly sophisticated method that can easily be performed at home and would be difficult to prevent (where is equality?)
- Would SOC help Austrian women?
FROZEN EGG BANK Inc. Selling eggs v donation, + - compensation (eg 900 euros, egg sharing..)

Basic Package (6 eggs)………. $15,000
Premium Package (12 eggs)….. $25,000

Recommendations (Ethics and Law TF)

- Should be available to those who want to “protect their reproductive potential against the threat of time”
- Offer in expert centres and not raise false hopes, with personalised information
- Explain relatively new, little follow up offspring and long term safety
- Policy makers to consider how to compensate women who have stored oocytes at time of use
- Freeze and share: counsel re gametes donation implications
- ART professionals promote and contribute age awareness in fertility matters
References


Mertes and Pennings (2011): Social egg freezing: for better, not for worse. RBM Online 23: 824-829


You can now register for these upcoming ESHRE Campus events:

- Application and challenges of emerging technologies in preimplantation and prenatal diagnosis
  12-13 September 2013 - Prague, Czech Republic

- Female genital tract congenital malformations: new insights in an old problem
  27-28 September 2013 - Thessaloniki, Greece

- Introducing new techniques into the lab
  4-5 October 2013 - Barcelona, Spain

- Polycystic ovary syndrome: A new look at an old subject
  25-26 October 2013 - Rome, Italy

- Infections from conception to birth: role of ART
  7-8 November 2013 - Berlin, Germany

- Endoscopy in reproductive medicine
  20-22 November 2013 - Leuven, Belgium

- From early implantation to later in life
  28-29 November 2013 - Brussels, Belgium

Mark your calendar for:

- Premature ovarian insufficiency
  6-7 December 2013 - Utrecht, The Netherlands