Q1: Do cancer survivors want to have children?

- Many young survivors have not started or completed a family
- Majority of survivors wish to have children
  - 76% of childless survivors
  - 80% felt “the cancer experience” makes them better parents
  - 90% felt healthy enough to be a good parent

- “Having children” ranked top 3 among various life goals from cancer patients aged 13-22 yrs

<table>
<thead>
<tr>
<th>Rank</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Health</td>
</tr>
<tr>
<td>2</td>
<td>Work/School</td>
</tr>
<tr>
<td>3</td>
<td>Having children</td>
</tr>
<tr>
<td>4</td>
<td>Romantic relations</td>
</tr>
<tr>
<td>5</td>
<td>Close friends</td>
</tr>
<tr>
<td>6</td>
<td>Faith</td>
</tr>
<tr>
<td>7</td>
<td>Nice home</td>
</tr>
<tr>
<td>8</td>
<td>Money</td>
</tr>
</tbody>
</table>

(Schover et al. 1999)  
(Klosky et al., 2014)
Q2: What impact are we talking about?

- **Semen parameters** ↓  (Chan et al., 2006)
  
  - Sperm aneuploidy?
    - Multi-color FISH
  
  - Impaired sperm DNA Integrity?
IMPACT OF CHEMOTHERAPY ON SPERM

• Increased aneuploidy frequencies at all time points for all investigated chromosomes:
  Testis cancer (TC) (n=12), Hodgkin’s lymphoma (HL) (n=11)
  - 0 months
    • HL (nullisomy 21), TC (disomy 21)
  - 6 months
    • HL and TC (XY disomy; nullisomy 13 & 21)
  - 12 months
    • HL (nullisomy 13)
  - 18-24 months
    • TC (disomy 13 and XY)
    • HD (disomy 21 and nullisomy 21)
SPERM DNA FRAGMENTATION (O’Flaherty et al., Fertil Steril. 2010)

10% DFI best distinguishes infertile vs community controls

Chemotherapy

Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update

**Abstract**

Purpose: To provide current recommendations about fertility preservation for adults and children with cancer.

Methods: A systematic review of the literature published from January 2013 to March 2017 was completed using PubMed and the Cochrane Library. An Update Panel reviewed the identified publications.

Results: There were 81 publications identified and reviewed. None of these publications prompted a significant change in the 2013 recommendations.

Recommendations: Health care providers should initiate the discussion on the possibility of infertility with patients with cancer treated during their reproductive years or with parents/guardians of children as early as possible. Providers should be prepared to discuss fertility preservation options and/or refer all potential patients to appropriate reproductive specialists. Although patients may be focused initially on their cancer diagnosis, providers should advise patients regarding potential threats to fertility as early as possible in the treatment process so as to allow for the widest array of options for fertility preservation. The discussion should be documented. Sperm, ovary, and embryo cryopreservation are considered standard practice and are widely available. There is conflicting...
Q3. How to set up a successful male fertility preservation program?

- Only 15-30% bank sperm. <60% recalled option discussed.  
  *(Magelssen et al., Eur Urol. 2005)*

- What factors influence the decision of sperm banking?

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Facilitators and obstacles to sperm banking in young men receiving gonadotoxic chemotherapy for cancer: the perspective of survivors and health care professionals

*Human Reproduction Vol.20, No.7 pp. 2106–2116, 2006*

FACILITATORS AND OBSTACLES TO SPERM BANKING IN YOUNG MEN RECEIVING GONADOXIC CHEMOTHERAPY FOR CANCER: THE PERSPECTIVE OF SURVIVORS AND HEALTH CARE PROFESSIONALS

Marie A. Achille, Zeev Rosberger, Roxane Robitaille, Sophie Lebel, Jean-Philippe Gouin, Barry D. Bultz, and Peter T.K. Chan

Department of Psychology, University of Montreal, Montreal, Quebec; *M.D. Hospital, McGill University, Montreal, Quebec; Behavioral Sciences and Health, University Health Network, Toronto, Ontario, Department of Psychosocial Research, Tom Baker Cancer Center, Calgary, Alberta; Faculty of Medicine, University of Calgary, Calgary, Alberta; and Department of Urology, McGill University Health Center, Montreal, Quebec.

*To whom correspondence should be addressed at: Department of Psychology, University of Montreal, 96 Vincent D'Urso, Montreal, Quebec, H3C 3V9. E-mail: marie.achille@umontreal.ca*

**BACKGROUND:** Testicular cancer and Hodgkin's disease are among the most common malignancies to affect young men of reproductive age. Although both are associated with high rates of infertility, sperm banking (SB) remains underutilized by both diagnostic groups. Reasons for this remain elusive. **METHODS:** This study used a qualitative design. In-depth interviews were conducted with 28 cancer survivors and 18 health care professionals (HCPs) to examine their perspectives on factors that facilitate or hinder SB. Interview data were analyzed using a mixed approach and a three-step process of data reduction, data display and conclusion drawing and verification. **RESULTS:** Eight factors were identified as having an impact on SB, and findings suggest that effective promotion of SB involves adequate communication around the severity and personal risk for infertility, assessing the importance of patients’ place on leaving children, emphasizing the benefits of SB and addressing possible obstacles such as cost.
Q3. How to set up a successful male fertility preservation program?

- Banking presented as part of standard of care by a knowledgeable healthcare professional
- Low cost

(Achille et al., Hum Rep, 2008; Herrero et al., Current Oncology, 2016)
Q3. How to set up a successful male fertility preservation program?

• Banking presented as part of standard of care by a knowledgeable healthcare professional
• Low cost
• Perception about simplicity and efficacy of banking
• Positive attitudes about survival
• Involvement of a parent or partner
• Fatherhood status
• Perception of fatherhood
• Cultural/sexual orientation

(Achille et al., Hum Rep, 2008; Herrero et al., Current Oncology, 2016)

Q4: How to handle adolescents?

• Sperm banking requires:
  Ability to ejaculate
  Spermatogenesis

Legality issues on consent
Legality issues on ownership

• How to “counsel” a teenager with cancer to masturbate for banking?
  Teens nowadays maybe more mature that we think!
Q4: How to handle adolescents?

- Sperm banking requires:
  - Ability to ejaculate
  - Spermatogenesis

- How to “counsel” a teenager with cancer to masturbate for banking?
  - Teens nowadays maybe more mature that we think!
  - But don’t assume they all can do it.....

Peter Chan M.D.
Q5: What procedures can be used to obtain sperm?

- Penile Vibratory stimulation
- Electro-ejaculation
Q5: What procedures can be used to obtain sperm?

- Penile Vibratory stimulation
- Electro-ejaculation
  - Anesthesia required
  - Risks of rectal injury
- Testicular sperm extraction
  - Anesthesia required
  - Risks of hematoma
  - Invasiveness vs yield

Q6: What option do we have for pre-adolescents?

- Sperm banking remains the only feasible option to preserve male fertility before chemotherapy
- If no spermatozoa, not much can be done
Can spermatogonial stem cells be isolated and preserved?

Spermatogonial stem cells exist since birth

If isolated before chemotherapy, they can be transplanted back to seminiferous tubules to restart spermatogenesis

This is fertility “restoration” (beyond just preservation)
Culturing Human Spermatogonia

Cycle of spermatogenesis
Mouse - 35 days
Rat - 55 days
Human - 60 days

Q7: What if no sperm were banked in an azoospermic survivor?

Testicular Sperm Extraction Combined with Intracytoplasmic Sperm Injection in the Treatment of Men with Persistent Azoospermia Postchemotherapy

Cancer 2001 92:1632
Q7: What if no sperm were banked in an azoospermic survivor?

- Testicular microdissection
- Postchemotherapy azoospermia

<table>
<thead>
<tr>
<th>Duration of azoospermia</th>
<th>16.3 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm retrieval rate</td>
<td>45%</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>80%</td>
</tr>
<tr>
<td>Pregnancy rate</td>
<td>45%</td>
</tr>
</tbody>
</table>


Peter Chan M.D.

Q8: Do banked sperm in cancer survivors work?

Assisted reproductive outcomes of male cancer survivors

Ainhoa García · María Belén Herrero · Hananel Hodier · Togus Tulandi · Peter Chan

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Abstract

Purpose: The objective of our study was to evaluate the reproductive outcome of male cancer survivors treated with intracytoplasmic sperm injection (ICSI) using cryopreserved sperm and compare it with the same treatment in non-cancer maligns.

Methods: We retrospectively analyzed database derived from cancer and non-cancer patients undergoing sperm cryopreservation from August 2008 to August 2012 at a university-based center. We evaluated the reproductive outcome of those cancer cohort was 62.1%, which was higher than that of the normospermic non-cancer population (p<0.0047).

Conclusions: The use rate of cryopreserved sperms from oncocoitertegy preservation cases is at around 10%. The live birth rate using assisted reproductive technologies among these patients is at least comparable to that of the non-cancer population.

Implications for Cancer Survivors To our knowledge, this was the first comparative study of male cancer survivors treated with ICSI using cryopreserved sperms, which were
Q8: Do banked sperm in cancer survivors work?

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cancer</th>
<th>Normospermic</th>
<th>Oligospermic</th>
<th>TESE</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive outcomes</td>
<td>1.5</td>
<td>1.5</td>
<td>1.3</td>
<td>1.9*</td>
<td>0.036</td>
</tr>
<tr>
<td>Number of embryos transferred</td>
<td>1.7</td>
<td>1.3</td>
<td>1.1</td>
<td>1.5</td>
<td>ns</td>
</tr>
<tr>
<td>Cumulative pregnancy rate (%)</td>
<td>68.9</td>
<td>37.1</td>
<td>52.6</td>
<td>60</td>
<td>0.0047</td>
</tr>
<tr>
<td>Cumulative live birth (%)</td>
<td>62.1</td>
<td>18.4</td>
<td>40</td>
<td>ns</td>
<td></td>
</tr>
<tr>
<td>Spontaneous abortions (%)</td>
<td>5.0</td>
<td>10.3</td>
<td>5</td>
<td>11.4</td>
<td>ns</td>
</tr>
</tbody>
</table>

With ICSI, banked sperm from cancer survivors performed at least as well as banked sperm from non-cancer patients

Reproductive healthcare professionals should inform oncological specialists of these findings when counselling new cancer patients

A 31 year-old man who received high-dose chemo for non-Hodgkin’s lymphoma 5 yrs ago and is now azoospermic. He banked his sperm prior to chemo twice (sperm counts 10 x 10^6/ml, 5% total motility). He had undergone two failed ICSI cycles with his 33 year-old reproductively healthy female partner (60% fertilization rate, grade b and c embryos).

Q9: What if banked sperm failed ICSI

A 31 year-old man who received high-dose chemo for non-Hodgkin’s lymphoma 5 yrs ago and is now azoospermic. He banked his sperm prior to chemo twice (sperm counts 10 x 10^6/ml, 5% total motility). He had undergone two failed ICSI cycles with his 33 year-old reproductively healthy female partner (60% fertilization rate, grade b and c embryos).
Q9: What if banked sperm failed ICSI

- Many cancer patients have elevated sperm DNA fragmentation even before chemotherapy
Q9: What if banked sperm failed ICSI

- Many cancer patients have elevated sperm DNA fragmentation even before chemotherapy
- Sperm cryopreservation may further increase sperm DNA damage

**IMPAIRED SPERM CHROMATIN STRUCTURE ON CRYOPRESERVED SPERM**

- SCSA®: DFI 76.6%  
  TUNEL: 72.5%
- Magnetic-activated cell sorting (MACS)  
  → Elimination of sperm showing apoptotic features
Q9: What if banked sperm failed ICSI

IMPAIRED SPERM CHROMATIN STRUCTURE ON CRYOPRESERVED SPERM

- SCSA®: DFI 76.6%
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- Magnetic-activated cell sorting (MACS)
  → Elimination of sperm showing apoptotic features

- Repeat ICSI with improved embryo qualities
  → Viable pregnancy

Peter Chan M.D. (with permission)
Q9: What if banked sperm failed ICSI

Case report: the use of annexin V coupled with magnetic activated cell sorting in cryopreserved spermatozoa from a male cancer survivor: healthy twin newborns after two previous ICSI failures

SUMMARY

- Cancer and its therapy have a significant negative impact on male reproductive health
- Sperm cryopreservation remains the only practical strategy for fertility preservation and must be offered to these patients
- Despite recovery of spermatogenesis, there are risks of damage to the gametes at the molecular level that may translate to adverse reproductive outcomes to these patients
- “Fertility after cancer” is an important and complex cancer survivorship issue. Proper counseling to these young patients prior to, during and after cancer treatment is essential to deliver optimal reproductive care with long-term satisfaction.
LATEST ADVANCES IN MALE FERTILITY PRESERVATION FOR CANCER PATIENTS

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