Oncofertility

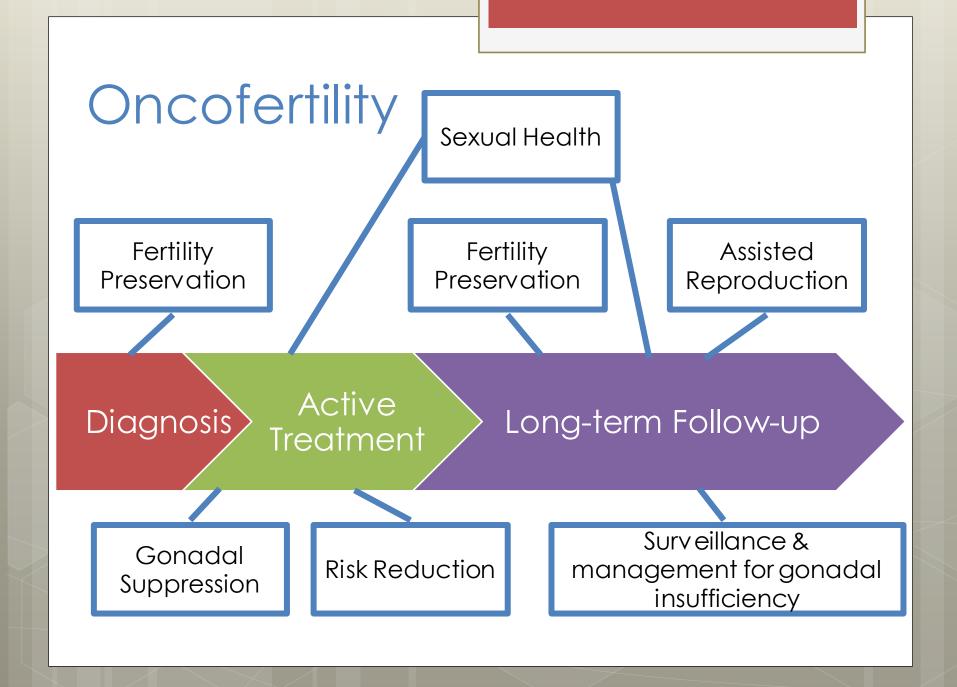
Kristin Marr, MHSc MD FRCPC October 17, 2024

Objectives

- Impart sufficient knowledge that you will feel prepared to:
 - Initiate discussion about fertility risks and preservation with newly diagnosed patients
 - Provide surveillance and care of patients following treatment with impacted fertility

Disclosure

- No conflicts of interest
- No shares in private clinics or fertility pharmaceuticals



Patient Perspective

"I was strong when I was faced with the diagnosis of cancer, treatment failures, life-threatening infection, and being near death, but the pain that I felt when I heard that my lifesaving cancer treatment would leave me infertile is impossible to describe."

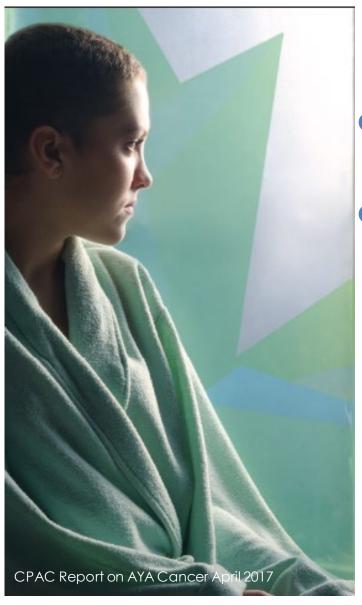
- Bronwen Garand-Sheridan, survivor, Manitoba

Patients want to know

- ~85% understand that chemo can impact fertility
- 50% feel that concerns are addressed
- <10% undergo fertility preservation</p>
- Even if nothing is possible, patients want to be referred for counseling

Partridge JCO 2004; Quinn JCO 2009; Yee J Ass Rep Gen 2016

Stage: New Diagnosis



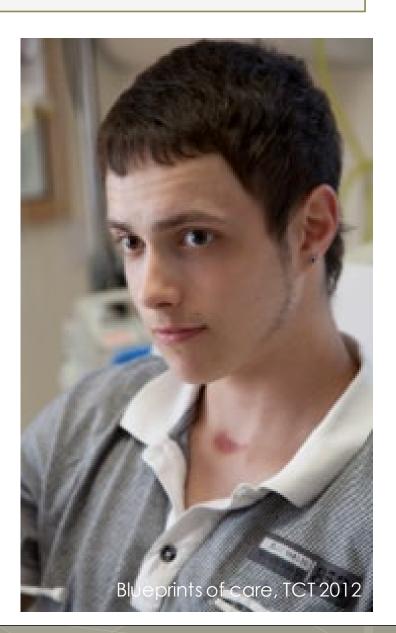
Ms F.

- Localized pelvic rhabdomyosarcoma
- Treatment:
 - Vincristine, Dactinomycin, Cyclophosphamide for 42 weeks
 - Total Alkylator dose: 30 g/m2
 - Pelvic surgery
 - Radiation therapy 36 Gy to primary site

"Will I still be able to have kids?"

Mr M.

- Testicular germ cell tumour
- Treatment:
 - Surgical resection
 - Bleomycin, Etoposide, Cisplatin



"You want me to do WHAT?"

Counseling on Risk of Infertility and Fertility Preservation

Clinical Practice Guidelines

VOLUME 36 · NUMBER 19 · JULY 1, 2018

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

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

Kutluk Oktay, Brittany E. Harvey, Ann H. Partridge, Gwendolyn P. Quinn, Joyce Reinecke, Hugh S. Taylor, W. Hamish Wallace, Erica T. Wang, and Alison W. Loren



PRACTICE GUIDELINE

Fertility preservation in reproductive-age women facing gonadotoxic treatments

CHILDREN'S ONCOLOGY GROUP J. Roberts MD,* R. Ronn MD,† N. Tallon MB BCh BAO,* and H. Holzer MD‡
The WCHA'S CHITATIONA
Cancer experts

Guideline for Fertility Preservation for Patients with Cancer

ASCO Recommendations

- All patients should receive counseling regarding fertility and preservation
- 2. Refer patients who express interest in preservation to a reproductive specialist
- 3. Address fertility asap, before treatment
- 4. Document discussion

Why is it not discussed?

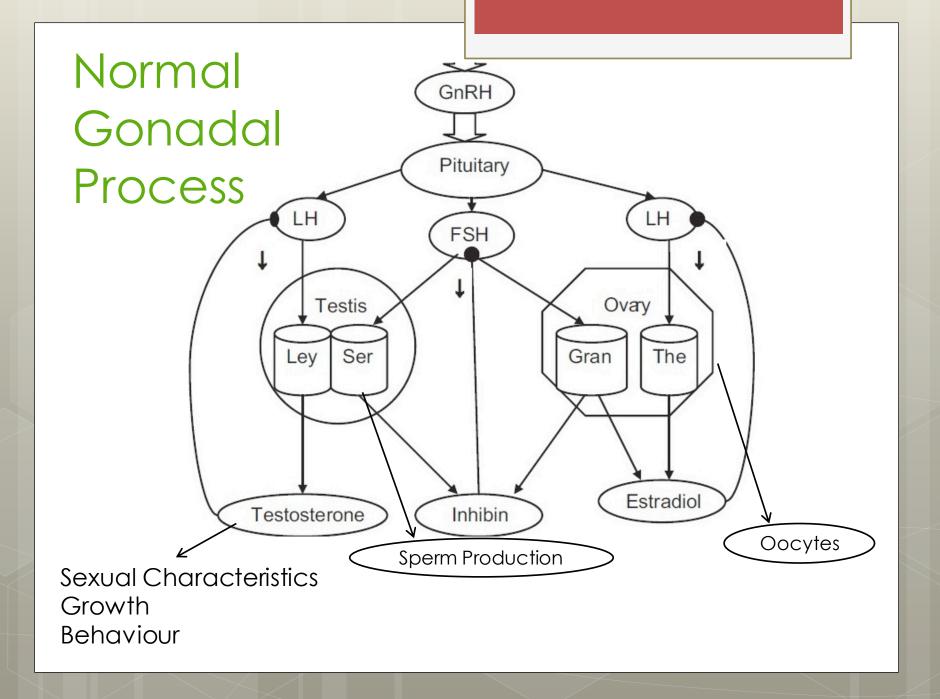
- Discomfort
- Lack of knowledge
- Patient too sick
- Not felt to be relevant to patient
- No preservation option available anyways
- Communication barriers
- Time constraints / priorities

Estimating Risk of Infertility

Chemotherapy

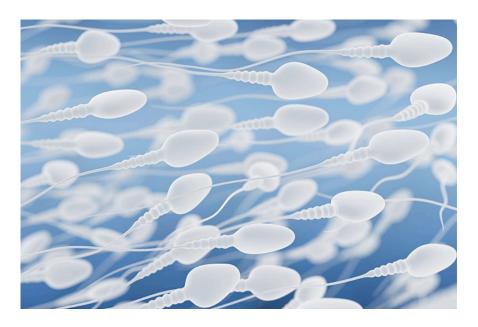
Surgery

Radiation Therapy



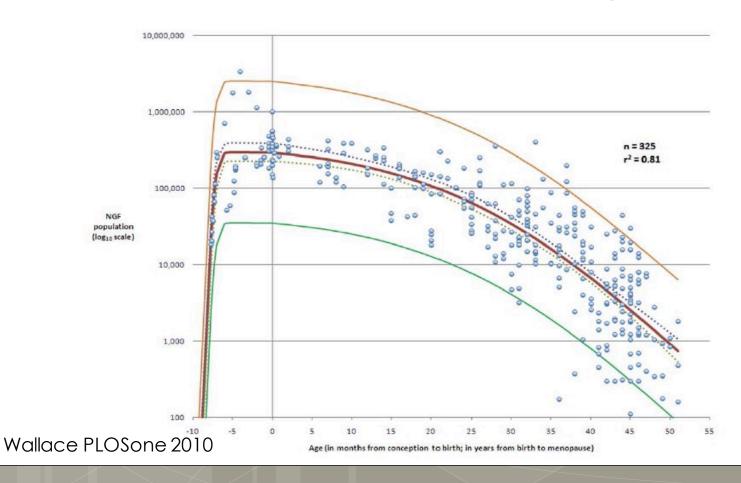
Spermatogenesis

- Starts only at onset of puberty
- 3 billion sperm / month, 100 per heart beat!!
- Sperm maturation time =74 days
- Continue to generate sperm until late in life

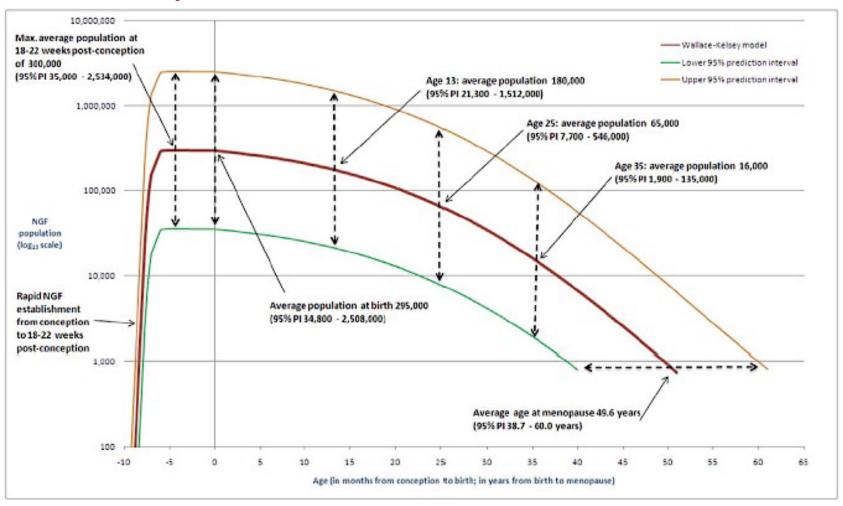


Oocyte Production

Born with finite number of oocytes



Menopause



Chemotherapy

Risk of Prolonged Oligospermia or Azoospermia

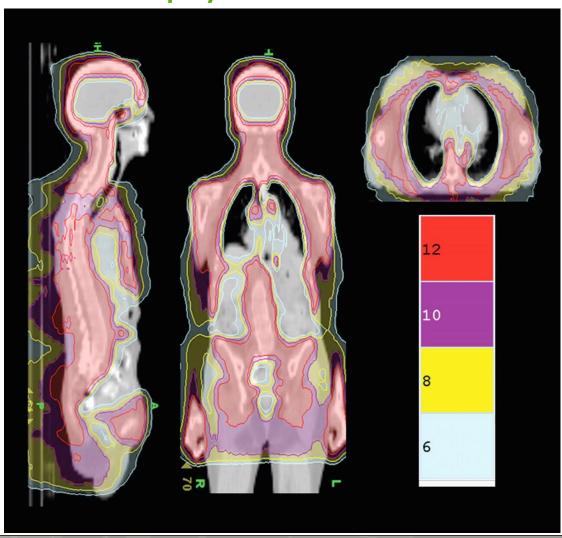
Agent	Possible Risk	High Risk
Cyclophosphamide	> 4 g/m ²	> 7.5 g/m ²
Busulphan		> 600 mg/m ²
Melphalan		> 140 mg/m ²
Ifosfamide	> 42 g/m ²	> 60 g/m ²
Procarbazine	> 3 g/m ²	> 4 g/m ²
Chlorambusil		> 1.4 g/m ²
BCNU	> 300 mg/m ²	> 1 g/m²
CCNU		> 500 mg/m ²
Cisplatin	> 300 mg/m ²	> 600 mg/m ²
T ' DT		. 4000 0

Chemotherapy

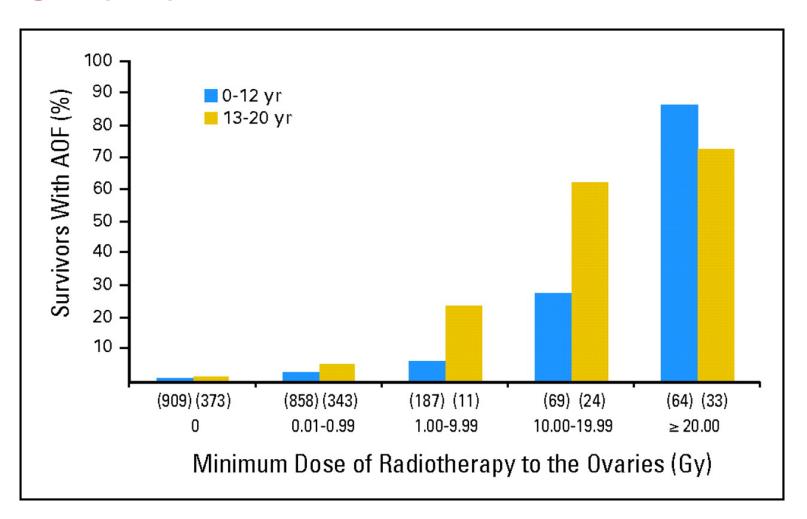
CED (mg/m2)	Risk Infertility in Individuals Assigned Male at Birth	Risk infertility in Individuals Assigned Female at Birth			
<4000	unlikely	unlikely			
4000-8000	40%	30%			
8000-20000	60%	50%			
>20000	90%	80%			

+/-up to 15%

Radiotherapy



Ovarian RT



Predicting Age at Ovarian Failure

Table 1. Predicted age at ovarian failure with 95% confidence limits for ages at treatment from 0 to 30 years and for doses 3, 6, 9, and 12 Gy

						-	r					
·:		3 Gy		6 Gy		9 Gy			12 Gy			
Age	Low	Mean	High	Low	Mean	High	Low	Mean	High	Low	Mean	High
0	31.2	35.1	39.0	18.7	22.6	26.5	9.8	13.7	17.6	4.0	7.9	11.8
1	31.3	35.2	39.1	19.0	22.9	26.8	10.4	14.3	18.2	4.8	8.7	12.6
2	31.5	35.4	39.3	19.3	23.2	27.1	10.9	14.8	18.7	5.5	9.4	13.3
3	31.6	35.5	39.4	19.7	23.6	27.5	11.5	15.4	19.3	6.2	10.1	14.0
4	31.7	35.6	39.5	20.1	24.0	27.9	12.1	16.0	19.9	6.9	10.8	14.7
5	31.9	35.8	39.7	20.5	24.4	28.3	12.7	16.6	20.5	7.7	111	15.5
6	32.1	36.0	39.9	20.9	24.8	28.7	13.3	17.2	21.1	8.4	12.3	16.2
7	32.2	36.1	40.0	21.3	25.2	29.1	13.9	17.8	21.7	9.1	13.0	16.9
17	34.3	36.4	42.1	43.9	29.8	33.1	20.5	24.4	46.3	17.0	20.3	24.4
18	34.6	38.5	42.4	26.4	30.3	34.2	21.2	25.1	29.0	18.0	21.3	25.2
19	34.9	38.8	42.7	27.0	30.9	34.8	21.8	25.7	29.6	19.0	22.0	25.9
20	35.1	39.0	42.9	27.5	31.4	35.3	22.5	26.4	30.3	20.0	22.8	26.7
21	35.4	39.3	43.2	28.0	31.9	35.8	23.2	27.1	31.0	21.0	23.5	27.4
22	35.7	39.6	43.5	28.6	32.5	36.4	23.9	27.8	31.7	22.0	24.3	28.2
23	36.0	39.9	43.8	29.1	33.0	36.9	24.6	28.5	32.4	23.0	25.0	28.9
24	36.3	40.2	44.1	29.7	2000	37.5	25.3	29.2	33.1	24.0	25.7	29.6
25	36.7	40.6	44.5	30.3	34.2	38.1	25.9	29.8	33.7	25.0	26.5	30.4
26	37.0	40.9	44.8	30.8	34.7	38.6	26.6	30.5	34.4	26.0	27.2	31.1
27	37.3	41.2	45.1	31.4	35.3	39.2	27.3	31.2	35.1	27.0	27.9	31.8
28	37.7	41.6	45.5	32.0	35.9	39.8	28.0	31.9	35.8	28.0	28.7	32.6
29	38.0	41.9	45.8	32.5	36.4	40.3	29.0	32.6	36.5	29.0	29.4	33.3
30	38.3	42.2	46.1	33.1	37.0	40.9	30.0	33.2	37.1	30.0	30.1	34.0

Wallace Int J Radiat 2005

Radiation to Uterus

- Uterus may be damaged by >10 Gy
 - Decreased uterine vasculature
 - Decreased muscular elasticity
 - Decreased growth (SGA) and positional abnormalities for fetus
 - Cervical incompetence and pre-term birth



Cranial Radiation

- >24Gy to anterior pituitary
 - Often causes gonadotropin (LH, FSH) deficiency
 - Delayed puberty or absent menses
- < 24Gy to Pituitary affects inhibition of GnRH
 - Premature release of GnRH and premature puberty

Delicate balance between the hypothalamus and pituitary is important and these patients are at risk for ovarian failure later on and they also have problems with maintaining pregnancy with early pregnancy losses.

Testicular Radiation

- Spermatogenesis is very sensitive to radiation
 - 0.1Gy can impair spermatogenesis
 - > 0.35Gy can cause permanent azoospermia
 - May have some recovery over a few years
- Leydig cells are more resistant
 - 2Gy in prepubertal
 - > >3Gy in mature males



Rowley Radiat Res 1974; Shalet J Endocrinol 1989

Fertility Preservation



Sperm

- Cryopreservation is standard of care
 - AKA Sperm Banking
- Offer to all patients > Tanner stage 3
- Often there is a low sperm count at diagnosis

"With ICSI, it only takes one!"

What to expect





STORAGE

Your sperm will be kept frozen until you decide to use or toss it

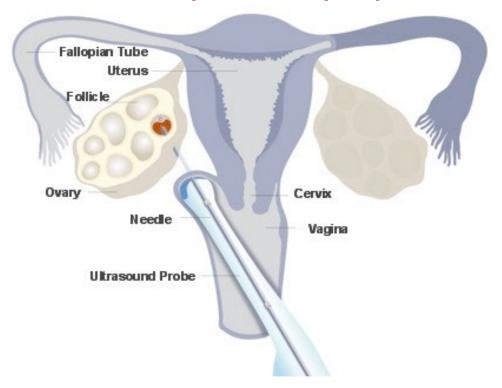
Alternatives

- Sperm aspiration
 - Testicular sperm extraction (TESE)
 - Can be used if patient too unwell for semen collection or if few sperm present
 - Access is limited
 - Percutaneous epididymal sperm extraction (PESA)
- Electroejaculation

Pre-pubertal

- No spermatogenesis
- Testicular tissue cryopreservation or reimplantation
 - Considered experimental
 - No mature sperm present
 - There is no technology as yet available to stimulate in vitro spermatogenesis
 - Theoretical autologous re-implantation
 - Offered only in specialized centres (Sick Kids)

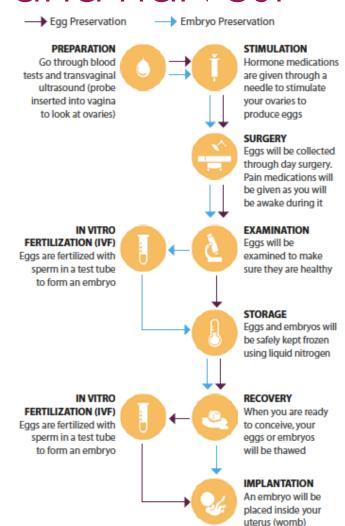
Embryo or Oocyte Cryopreservation



Since October 2012, freezing of unfertilized egg is no longer considered experimental

Oocyte stimulation and harvest

- Optimal stimulation within 3 days of start of cycle, but random stimulation shown to be successful too
- Length of process now ~12 days



Rates of success

Number of eggs frozen	Chance of live birth*
5	15%
10	61%
15	85%

^{*}For women who froze their eggs at age 35 or younger.

 Successful IVF with oocytes almost equivalent to embryo

FP and breast cancer

- GnRH antagonists will create supraphysiologic spike in estradiol.
- Co-administration with aromatase inhibitor (letrozole) allows harvest of mature oocytes while maintaining low estradiol levels
- Similar efficacy of oocyte yield, maturation and fertility rates
- Off-label use and minimal data on impact on breast cancer outcomes

Ovarian Tissue Cryopreservation

- One ovary is laparoscopically removed. Small strips of ovarian cortex are processed and individually frozen for future use.
- Segments of ovarian tissue can be re-inserted surgically (autotransplantation), and will resume hormone production and oocyte production in vivo. This can result in natural pregnancy.
- Alternately, oocytes may be matured in-vitro for use with IVF assisted reproduction
- Benefits: No hormone stimulation, no delay in therapy, can be done any age
- Cons: Surgical procedure, loss of an ovary, access

No longer considered experimental since 2019

Challenges in young patients

	Egg/Embryo Freezing	Ovarian Tissue Cryopreservation	Limitations/ Considerations with OTC
Relationship status	No longer an issue with oocyte cryopreservation	No fertilization required	
Pre- or peri-pubertal.	Unable to stimulate mature egg production	Can be done at any age. Tissue function resumed upon reimplantation	No successful cases of pregnancy in pre- pubertal tissue
License/Access.	Sedation at fertility clinics now based on weight, which allows access for younger patient	Procedure can be performed at pediatric centre by Pediatric Gynecology and Pediatric Anaesthesiology	Considerable logistical coordination required. Embryologist must be present to process tissue.
Not sexually mature or sexually active	Undergoing transvaginal ultrasounds and procedures are too invasive	Laparoscopic procedure done at time of other surgeries. No transvaginal process.	Ethical considerations of ovary removal.

Barriers to Fertility Preservation



Reproductive Medicine Services and Clinics

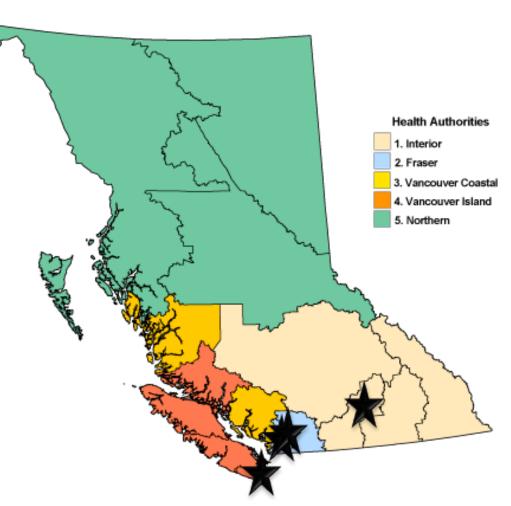
Health region dependent

Primarily private in BC

Geographic access

 Multiple clinics offer fertility services

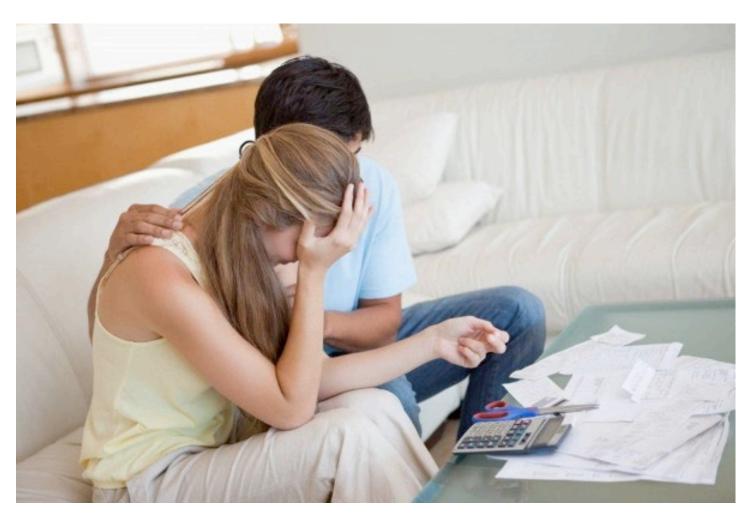
 5 2 offer full IVF services; one preserves ovarian tissue



Logistic Barriers

- Physically unwell patient
 - Transporting sample
 - Traveling to clinic
- Multiple attempts may be required
- Delays in start of treatment to organize appointments or await oocyte stimulation
- Age & maturity
 - Unable to undergo oocyte stimulation; transvaginal procedures too invasive; clinics can only sedate above specific weight
- Technology
 - Can harvest oocytes/tissue at hospital, but no technology to freeze and transport

Financial Barriers



Financial

	Cost
Consultation by Reproductive Medicine	MSP
Sperm banking	\$800
Additional sperm sample	\$200
Surgical sperm retrieval	\$2350
Yearly storage fee	\$350
In Vitro Fertilization	\$8500
Intrauterine Insemination	\$600

Financial

Source: PCRM Sept 2019

	Cost
Consultation by Reproductive Medicine	MSP
Embryo or Egg stimulation & preservation	\$7600
Hormone Medication	\$3000-7000
Yearly storage fee	\$400
Re-implantation of embryo	\$6000
In Vitro Fertilization	\$8500
Frozen donor egg (total fees)	\$24,000

Financial Assistance

- 1. Extended health
 - ~15% of patients have coverage for medications
- Compassionate access
 Pharma "gifts" access to medications (\$4000-5000)
- 3. Clinic discounts

Agreement among clinics to charge maximum of \$4000 for egg/embryo cryopreservation, and \$350 for sperm freezing

4. Not-for-profit Organizations

With proof of financial need, can provide up to \$2000 for egg/embryo cryopreservation and 1 year of storage; and \$350 for sperm freezing

http://fertilefuture.ca/programs/power-of-hope/

Financial Assistance

Limitations

- Clinics must agree (All participate in BC)
- Women: End cost of \$2000
- There are strict household income criteria to qualify
- Not covered:
 - Blood tests, annual storage, implantation

New Patient Counseling

First Visit

- Screening Q "Cancer therapy can impact sexual health and fertility. Would you like to speak to someone about this topic?"
- Resources
- Referral for counseling and/or fertility preservation

Prechemo

- Patient-specific counseling regarding impact of disease and treatment on sexual health and fertility; options for preservation
- Resources
 - Referral for counseling and/or fertility preservation

During Treatment

- Support for sexual health
- Possible option for fertility preservation
- Prepare for monitoring and support after completion of treatment

Resources



Adolescent & Young Adult Cancer Care & Support

Every year in Canada, over 8,300 Adolescents and Young Adults (AYA), ages 15-39, are diagnosed with cancer. AYAs have unique needs and challenges. Below is a collection of resources to help navigate these challenges and get support.

More Resources



bccancer.bc.ca/health-info/coping-with-cancer/managing-symptoms-side-effects/sexual-health

Our Services

Menu =



Follow us 🔝 Contact About

anew

There is an urgent need to reshape young adult cancer care for all young adults.

Every year in Canada nearly 8,300 young adults aged 15-39 are diagnosed with cancer.

LEARNING & RESOURCES

That is nearly 1 young adult diagnosed every 65 minutes or more than 20 young adults diagnosed every day.

Sexual Health

Health Info

Cancer diagnosis, treatment, and recovery can impact sexual health in many ways. Check out the information and resources below.

Health Info / Coping with Cancer / Managing Symptoms & Side Effects

Our Research

How to refer

- Currently two REI clinic offer full services
 - Pacific Centre for Reproductive Medicine (PCRM)
 - Olive Fertility Centre
- Referrals are triaged and key words related to cancer therapy prompt urgent appointment within a few days
- Direct email with REI physicians
- No referral required patients can book with clinic directly

, , , , , , , , , , , , , , , , , , ,				
C @ 5 olivefertility.com/referring-physicians Recation-svancouver	*	pacificfertility.ca/refer-a-patient		
Step 1: Select Olive Location		PCRM The Prelude Network	Start Your Journey Services Medications Financial Resources About Contact	
Vancouver	~			
Step 2: Complete the online form or download a printable referral form you can fax to us		We're here to support your patients.		
Online Form		We welcome your referrals and strive to provide the best possible fertility care for your patients. Please download the form or fill out the fields below, and a member of our team will be in touch shortly.		
Get Printable Form		PCRM Fertility Referral Form Fax to: 604-434-5522		

During Active Treatment

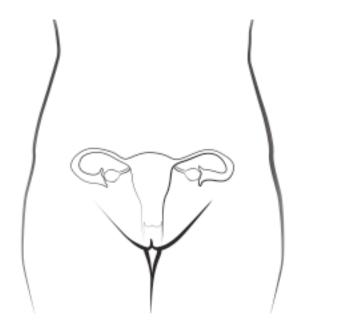
How can we protect against or minimize impact?

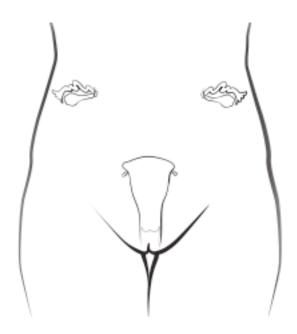
Risk-reduction chemotherapy strategies

- Minimize exposure to gonodotoxic chemotherapy by:
 - Use of alternate agents
 - Response-based protocols with riskadapted treatment
 - Increase number of agents used, with overall lower cumulative doses of each agent

Prevent RT exposure to gonads

- Testicular shielding
- Oophoropexy (ovarian transposition)





GnRH Agonists

- Insufficient evidence of benefit for fertility preservation
- Not universally recommended "but could be considered if no proven preservation option possible"
- Potential additional benefit of menstrual suppression during times of low platelets

Sexual Health & Sexual Identity

Consider needs of all patients



Resources for LGBTQ2S+ Cancer Patients

BC Cancer Patient & Family Counselling



Patient and Family Counselling:

www.bccancer.bc.ca/our-services/services/supportive-care/patient-family-counselling

BC Cancer Support Programs: www.bccancer.bc.ca/supportprograms
Individuals, couples, caregivers and families can talk to our counsellors in-person or over the phone, or attend counsellor-led support groups at our regional centres.

BC Cancer Library Materials

www.bccancer.ca/library

Advocate guide to gay men's health and wellness

by Frank Spinelli (Book)

Personal Stories

Cancer's Margins www.lgbtcancer.ca

Canada's first nationally-funded, national study of LGBT2Q experiences of cancer health and care, as well as support

Common concerns we can help with:

- Managing menopausal symptoms
- Vulvar and vaginal dryness
- Pain with sex or any genital touch, such as pelvic exams
- Questions about changes in sexual function
- Decreased sexual desire
- Changes in genital sensations and orgasm
- Talking about sexuality and intimacy with your partner

Contact information

Vancouver Sexual Health & Menopause Clinic

Call 604.877.6000 ext 672367

Fax 604.877.6179

BC Cancer – Vancouver 600 West 10th Avenue Vancouver, B.C.



Provincial Health Services Authority

Vancouver Sexual Health & Menopause Clinic

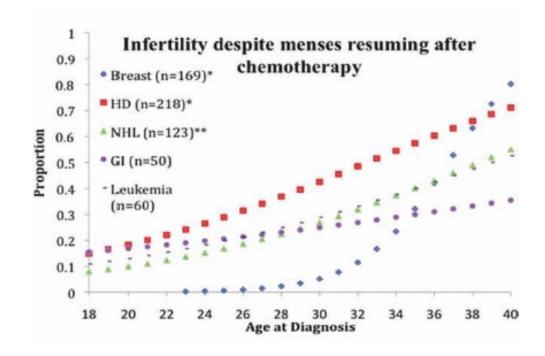


Free, confidential support for people with cancer and their partners

Post-Treatment

Assessing fertility potential

- Menses and LH/FSH are poor markers
 - Inconsistent levels, age dependent
 - Do not reflect ovarian reserve
 - Late markers of true ovarian failure
- Ovarian folliclecount is optimal

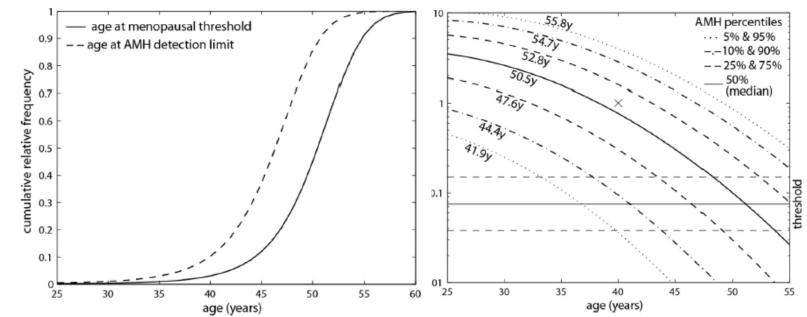


Letourneau Cancer 2012

Assessing fertility potential

Anti-Mullerian Hormone

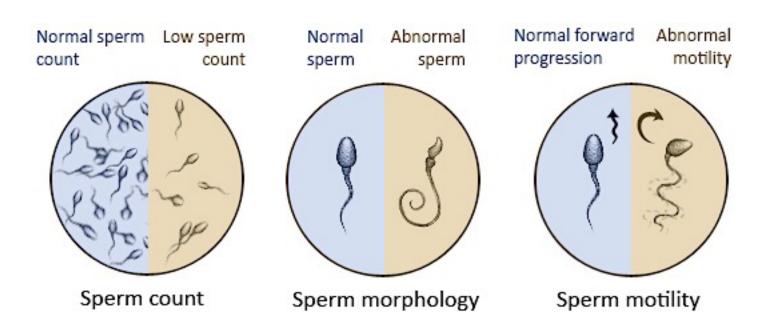
Dolleman J Clin Endo 2013



- Secreted by antral follicles and reflects ovarian reserve
- •Not covered by MSP → \$70

Assessing fertility potential

Sperm analysis



Instructions for Semen Collection

- Abstain for about 4 days prior to your specimen and keep the same abstinence interval for each specimen you provide (Ideally 7d)
- If you need more than one specimen, space them a few weeks apart
- Try and collect the specimen during a time when your wife is unlikely to be ovulating (e.g. during menstruation)
- Take your specimen to the laboratory as soon as possible, ideally within 1 hour of collection
- Keep the specimen warm by placing the collection container in a shirt pocket

High Risk of Early Gonadal Insufficiency

- Refer to Reproductive Medicine
 Specialist for full assessment
- Opportunity to undergo fertility preservation after completion of treatment
- Early family planning

Be careful what you tell your patients: risk of infertility is no excuse for lack of safe sex practices

Or you may have a new patient one year later.

Bottom Line

- ALL patients want and need to have fertility discussed before starting treatment
- If you don't feel qualified to carry out full discussion, then offer referral to reproductive endocrine clinic for consultation

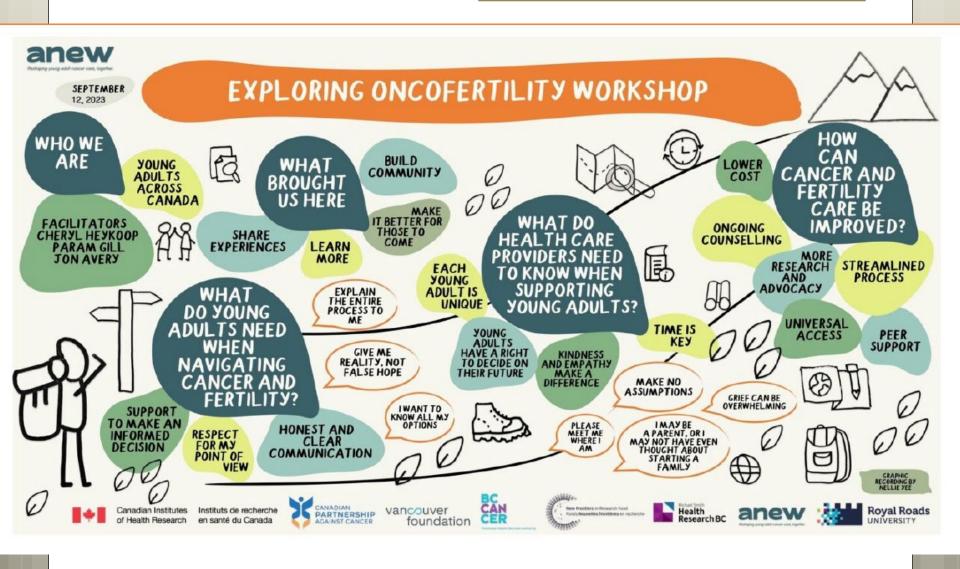
Fertility Preservation - A Top Priority for AYAs

- Potential fertility loss due to cancer treatment major issue for AYAs: adolescents and young adults (15-39)
- YAC Prime Study, 2020: Only 52% of AYAs had a conversation with their treatment providers about fertility preservation options. Only 13% went through preservation.
- Collaborative in BC/Yukon to ensure timely, equitable access to preservation services and effective resources
- CPAC, \$200K, 2 year-funded initiative with:
 - BC Cancer
 - BC Children's Hospital
 - Yukon Hospitals
 - Anew Research Collaborative @ Royal Roads University

"Nobody ever discussed fertility with me or if I ever wanted to have a family. It's awful to feel like you lost your future."

~AYA with lived experience with cancer





Next Steps

advocacy
personal experience
compiling learnings
building relationships

co-developing the ideal fertility care pathway

co-designing effective resources

Counselling pilot

Summit session: collaborative review & enhancement by AYAs and providers

reshaping AYA cancer care for the better

Hain Iu.

Thank Y Thank Y ThankY Thank Y

Join us @ the BC Cancer Summit

Fertility & AYA Cancer - Improving Options Nov 22, 2-3:30pm

Take in an Immersive Performance -Register for: Navigating AYA Cancer Care



Connect anytime: hello@anewresearch.ca anewresearch.ca