

# On Site Fertility Preservation Clinic

## An Update on the St. Jude Experience

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*Partner, Fertility Associates of Memphis*



St. Jude Children's Research Hospital was founded in Memphis by Lebanese entertainer Danny Thomas in 1962 to fulfill a promise that he made in a desperation prayer to St. Jude Thaddeus, one of the Twelve Apostles.



Danny Thomas  
Jan 6, 1912 – Feb 6, 1991

“No child should die  
in the dawn of life”

# Fertility Associates of Memphis (FAM)

## Timeline to Fertility Preservation Clinic at SJCRH

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- 1996 -FAM and SJCRH team up to freeze sperm
- 1998- Research affiliation to publish outcomes
- 2004- FAM joined Live Strong Fertile Hope
- 2009- FAM joined Oncofertility Consortium
- 2012- Initial plans for on-site clinic at SJ
- 2013- FAM live birth from frozen oocytes
  - First oocyte freeze for SJ patient
  - Clinical Privileges approved at SJCRH
- 2014- First on-site patients seen at SJ

# Primary Factors Encountered- Barriers to Oocyte Preservation

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1. Lack of information (patients/providers)
2. Access to treatment
3. An experienced fertility staff
4. Perceived delay in oncology treatments
5. Cost of fertility preservation treatments

Gorman JR, Bailey S, Pierce JP, Su HI. How do you feel about fertility and parenthood? The voices of young female cancer survivors. *J Cancer Surviv.* 2012 Jun;6(2):200-9.

Rodriguez-Wallberg KA, Oktay K. Options on fertility preservation in female cancer patients. *Cancer Treat Rev.* 2012 Aug;38(5):354-61.

Reh AE, Lu L, Weinerman R, Grifo J, Krey L, Noyes N. Treatment outcomes and quality-of-life assessment in a university-based fertility preservation program: results of a registry of female cancer patients at 2 years. *J Assist Reprod Genet.* 2011 Jul;28(7):635-41.

Quinn GP, Murphy D, Knapp C, Stearsman DK, Bradley-Klug KL, Sawczyn K, Clayman ML. Who decides? Decision making and fertility preservation in teens with cancer: a review of the literature. *J Adolesc Health.* 2011 Oct;49(4):337-46.

Goodman LR, Balthazar U, Kim J, Mersereau JE. Trends of socioeconomic disparities in referral patterns for fertility preservation consultation. *Hum Reprod.* 2012 Jul;27(7):2076-81.

Balthazar U, Deal AM, Fritz MA, Kondapalli LA, Kim JY, Mersereau JE. The current fertility preservation consultation model: are we adequately informing cancer patients of their options? *Hum Reprod.* 2012 Aug;27(8):2413-9.

# Barriers to Fertility Preservation

## 1.LACK OF INFORMATION: GOALS

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- SJCRH Fertility Preservation **information should be given to all new patients**
- On first visit ask if they have **any questions about future fertility** and refer to clinic
- **Seminars to Professional Providers** of care
- **Orientation of new staff** at SJCRH
- Visits to **all primary provider clinics**
- Information for the **community**

# The OncoFertility Consortium Seminars at St. Jude to Educate Staff

FAM was the only contributing oncofertility program within a 235 mile radius of Memphis



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Billy  
Kutteh

Amelia  
Bailey

Teresa  
Woodruff

James  
Klosky

Paul  
Brezina

# 2018: ASCO RECOMMENDATIONS-FEMALES

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Recommendation 1.1. People with cancer are interested in discussing fertility preservation. Health care providers caring for pediatric patients with cancer (including medical oncologists, radiation oncologists, hematologists, pediatric oncologists, surgeons, and others) **should address the possibility of infertility** as early as possible before treatment starts.

Recommendation 1.2. Health care providers **should refer patients** who express an interest in fertility preservation (and those who are ambivalent) to reproductive specialists.

Recommendation 1.3. To preserve the full range of options, fertility preservation approaches **should be discussed as early as possible**, before treatment starts.

Oktaay K et al, et al. Fertility preservation for Patients with Cancer. ASCO Clinical Practice Guideline Update. J Clin Oncol 36:1994-2001, 2018..

# 2018: ASCO RECOMMENDATIONS-FEMALES

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Recommendation 3.2. **Cryopreservation of unfertilized oocytes** is standard medical therapy. Oocyte cryopreservation should be performed in centers with the necessary expertise.

Recommendation 3.5 (updated). **Ovarian suppression when proven fertility preservation methods such as oocyte, embryo, or ovarian tissue cryopreservation are not feasible**, and in the setting of young women with breast cancer, GnRHa may be offered to patients in the hope of reducing the likelihood of chemotherapy-induced ovarian insufficiency.

Recommendation 3.6 (updated). **Ovarian tissue cryopreservation and transplantation:** Ovarian tissue cryopreservation for the purpose of future transplantation does not require ovarian stimulation and can be performed immediately.

Recommendation 4.1. All oncologic health care providers **should be prepared to discuss** infertility as a potential risk of therapy.

Oktaç K et al, et al. Fertility preservation for Patients with Cancer. ASCO Clinical Practice Guideline Update. J Clin Oncol 36:1994-2001, 2018..



## A Fertile Future

The new St. Jude Fertility Clinic offers options to some current patients, as well as to long-term survivors.

By Elizabeth Jane Walker

**F**ifteen-year-old Alexis Gilmore has a message for the children she may have years from now: "I loved you long before I ever knew you."

Cancer ravaged Alexis' reproductive organs when she was a toddler. After puberty, she was haunted by the possibility that she might never have children of her own.

"It really bothered me," Alexis says.

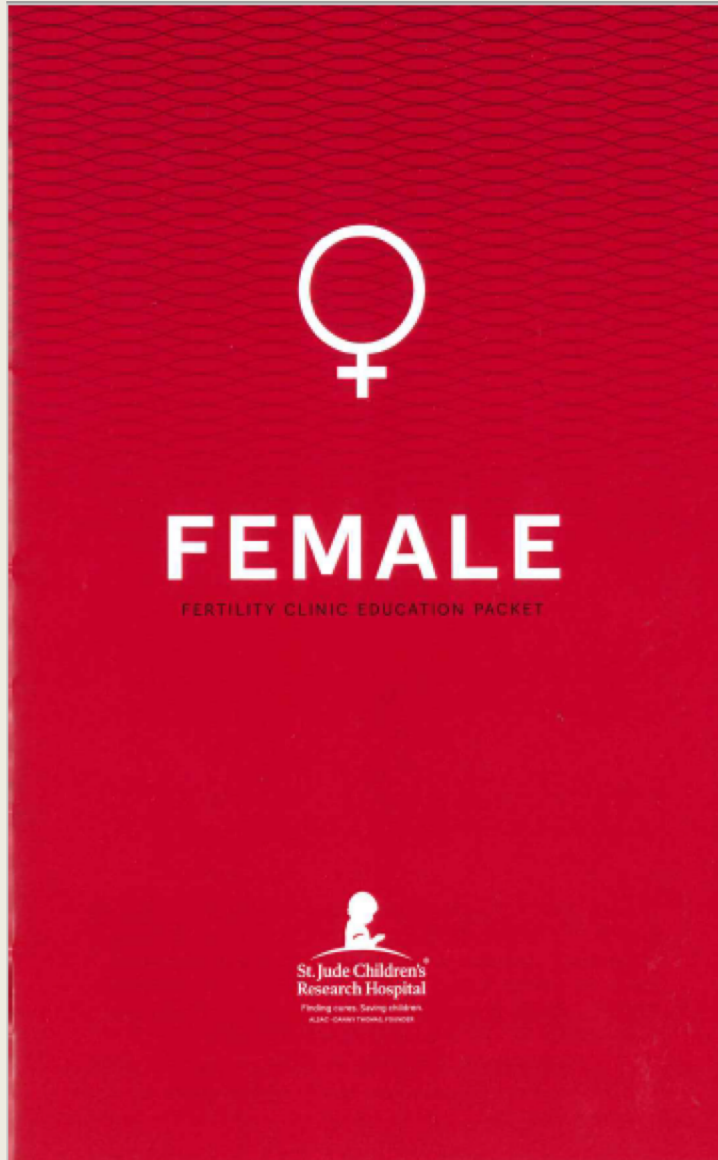
When St. Jude Children's Research fertility clinic for its patients in June of leapt. She knew that she was at high risk her uterus had been removed during cancer. One of her ovaries had already ceased to function. Doctors possibly harvest the eggs in her future use? She was determined to find

15 year old cancer patient kept a "Baby Book" of her oocyte cryopreservation cycle to show to her children someday. Article published in the quarterly SJ Promise Magazine.



While undergoing fertility preservation procedures at St. Jude, Alexis Gilmore created a baby book that she can show to her children someday.

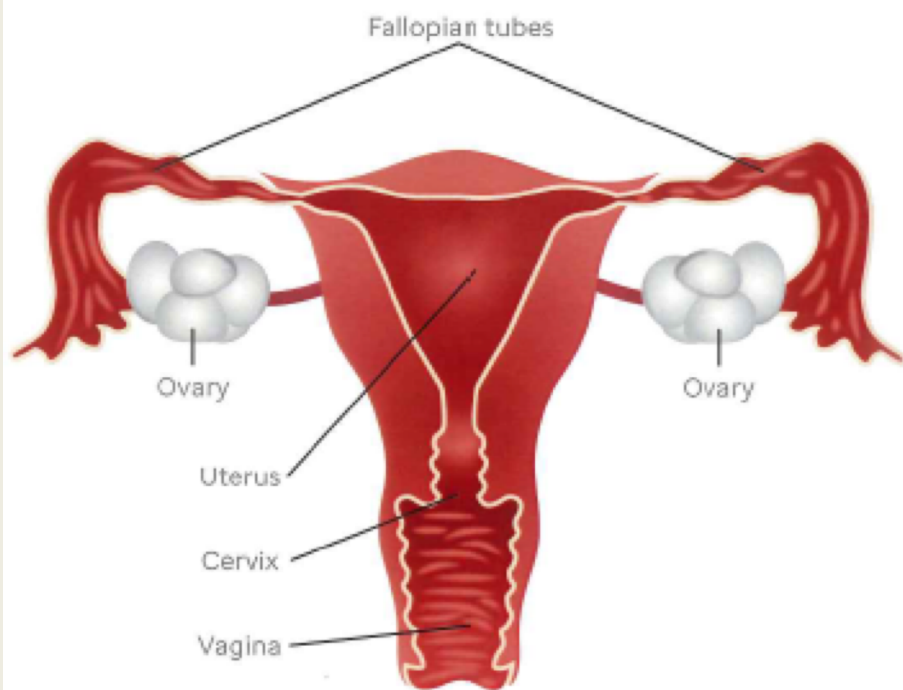
# Informational Booklet on Fertility Preservation for all patients who come to SJCRH



## Welcome to the Fertility Preservation Clinic

### Information for girls and women

Cancer and cancer treatment can affect your ability to have children later. However, you can do some things to increase the chance of having children if you want them. The Fertility Preservation Clinic at St. Jude can help. Planning ahead is important if you need cancer treatment.



The picture above shows a woman's reproductive system. This is the system that allows a woman to become pregnant and have a baby. Ovaries are where your eggs are stored. If you decide to freeze some eggs for later use, your doctor will take them from the ovaries.

## How cancer treatment affects fertility

Your eggs are the cells that join with a man's sperm to create a child. Women have 2 small organs in the lower belly called the ovaries (OH-vur-ees). When you are born, your ovaries contain all the eggs you will ever have. Chemotherapy and radiation are common cancer treatments, and they can be very effective. But they also cause long-lasting effects, including damaging your eggs or lowering the number you have. If so, you might not be able to have children.

**Fertility (fur-TILL-uh-tee)** means the ability to have children. For girls and women, this is the ability to become pregnant and have a baby.

## Preserving your eggs before cancer treatment

Freezing some eggs for later use could be your best option to become pregnant in the future. It is best to freeze eggs before you start cancer treatment. After treatment, it might not be possible to find enough eggs, or eggs that are still of good quality. Your doctor and cancer team can tell you if you qualify to have some eggs frozen before treatment.

## Understanding the AMH chart

The chart below shows the average AMH level for women at different ages. For example, if you are 18, and your AMH level is 3.86, you are at the 25 percent level for your age. This means 75 percent of women your age have a higher AMH level than you do, and 25 percent have a lower AMH level.

If you are 18, and your AMH is 12.90 or more, you are at the 95 percent level for your age. Only 5 percent of women your age have a higher AMH level than you.

Your AMH level is \_\_\_\_\_.

Your AMH level was tested on \_\_\_\_\_.

The table at the right is from the following article.

La Marca A, Spada V, Grisendi E, et al. Normal serum anti-Müllerian hormone levels in the general female population and the relationship with reproductive history. *European Journal of Obstetrics and Gynecology and Reproductive Biology* 2012;163(2):180-184.

## AMH Chart

Age	5%	25%	50%	75%	95%
18	1.74	3.86	5.891	8.40	12.90
19	1.67	3.73	5.729	8.23	12.74
20	1.59	3.60	5.566	8.05	12.58
21	1.52	3.47	5.404	7.86	12.40
22	1.45	3.34	5.241	7.68	12.23
23	1.39	3.22	5.078	7.49	12.04
24	1.33	3.09	4.916	7.31	11.85
25	1.26	2.97	4.753	7.11	11.65
26	1.21	2.85	4.590	6.91	11.44
27	1.15	2.73	4.428	6.72	11.23
28	1.09	2.62	4.265	6.52	11.01
29	1.04	2.50	4.102	6.31	10.78
30	0.99	2.38	3.940	6.11	10.54
31	0.94	2.27	3.777	5.90	10.29
32	0.89	2.16	3.615	5.68	10.04
33	0.84	2.05	3.452	5.47	9.77
34	0.79	1.94	3.289	5.25	9.49
35	0.75	1.84	3.127	5.03	9.21
36	0.70	1.73	2.964	4.80	8.91
37	0.66	1.63	2.801	4.57	8.59
38	0.62	1.52	2.639	4.34	8.27
39	0.58	1.42	2.476	4.11	7.93
40	0.53	1.32	2.313	3.86	7.57
41	0.49	1.22	2.151	3.62	7.20
42	0.45	1.12	1.988	3.38	6.82
43	0.42	1.03	1.826	3.13	6.41
44	0.38	0.93	1.663	2.87	5.98
45	0.34	0.84	1.500	2.61	5.53
46	0.30	0.74	1.338	2.35	5.07
47	0.26	0.65	1.175	2.09	4.57
48	0.23	0.55	1.012	1.81	4.04
49	0.19	0.46	0.850	1.53	3.49
50	0.15	0.38	0.687	1.26	2.91
51	0.12	0.28	0.525	0.95	2.29

## About the ultrasound test

Each of a woman's eggs is in a small, fluid-filled sac. This sac is called a *follicle* (FALL-ick-ul). An ultrasound test can show how many follicles you have. The egg in each follicle is too small to see with an ultrasound, but counting follicles helps your doctor learn how many eggs you probably have. (There is no guarantee that every follicle contains an egg.) Your follicle count and AMH test results tell the St. Jude team if you have enough eggs of good quality to freeze some.

## Using ultrasound to count follicles

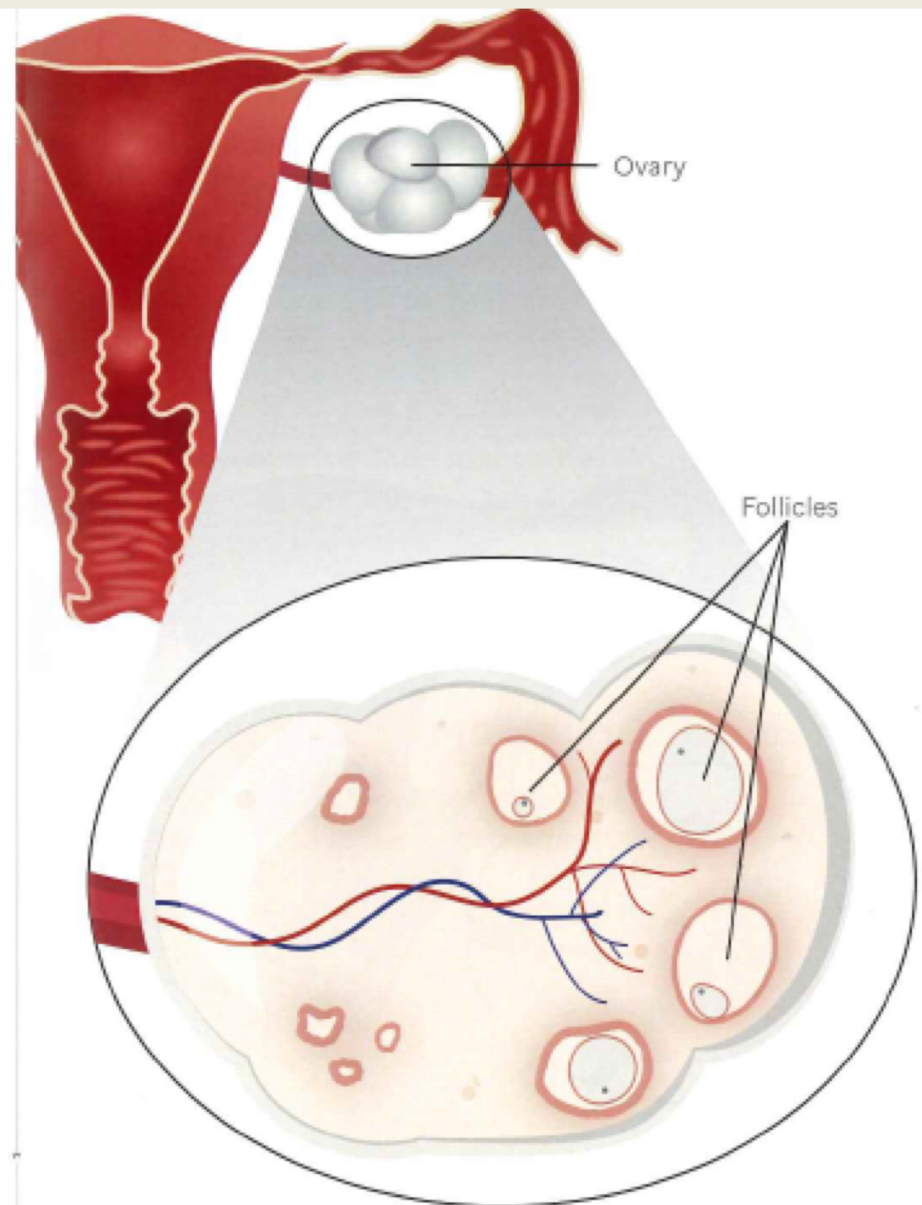
An ultrasound test uses sound waves to create pictures on a screen. You might be familiar with ultrasound from having a baby or having other tests. The test does not hurt. There are 2 ways to do an ultrasound to count follicles:

- A doctor puts an ultrasound probe in the vagina and counts follicles that way. This gives the best picture. The doctor can do it at a clinic appointment, and you get the results right away.
- A technician puts an ultrasound probe on the lower belly area and counts the follicles. This gives better results if the patient is not overweight. You need to schedule it separately from a clinic appointment. Your bladder needs to be full during the test, because this helps the technician see the follicles.

Your follicle count was \_\_\_\_\_ in the left ovary  
and \_\_\_\_\_ in the right ovary.

We found \_\_\_\_\_ total follicles.

You had a transvaginal / abdominal ultrasound on  
\_\_\_\_\_.



Each ovary contains small, fluid-filled sacs called follicles. The follicles contain eggs. The eggs cannot be seen with an ultrasound test, but your doctor can count the follicles to learn how many eggs you could have.

# Barriers to Fertility Preservation

## 2. ACCESS TO CARE

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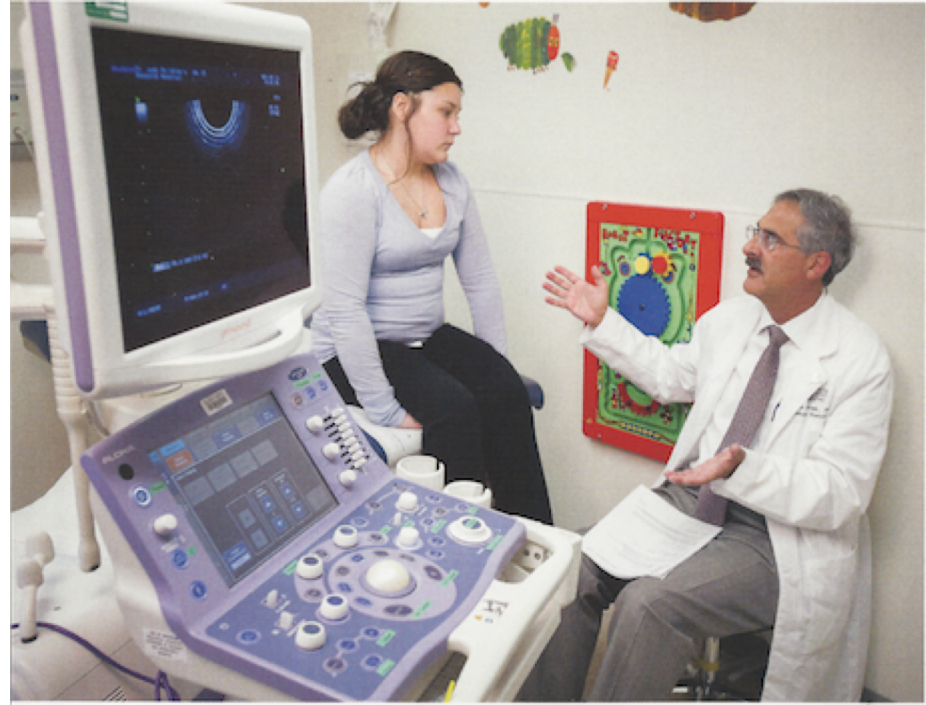
- 24/7 access 901-747-BABY (2229)
- Consult same day or next day
- Four board certified providers
- On Site Fertility Preservation Clinic



# On Site Facilities at SJCRH

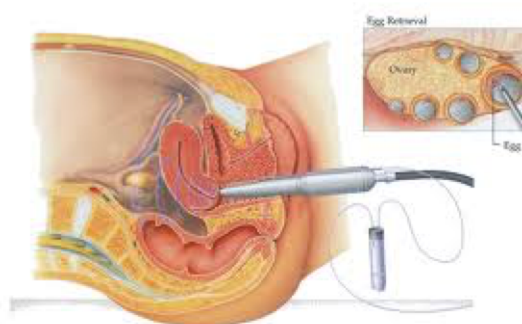


Initial Consult Room



Transvaginal Sonar Room

Antral follicle count  
(Abdominally when appropriate)



# Fertility Consultations for SJ patients: Number completed by FAM by Year

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	2012	2013	2014	2015	2016	2017	2018	2019 (Projected)
# New Patients	6	12	56	92	103	115	148	125
# Return Patients	0	1	40	68	77	96	111	124
# Phone Consults	0	0	15	46	52	84	146	150



On-Site Fertility Preservation Clinic Initiated

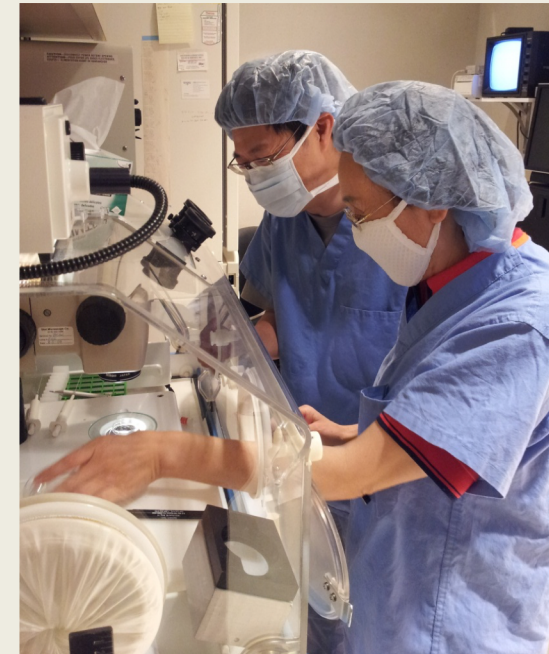


# Barriers to Fertility Preservation

## 3. EXPERIENCED FERTILITY CENTER

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- Laboratories experienced with egg freezing and warming
- Excellent vitrification program
- Successful egg donor program
- Staff available on lab breaks
- 24/7 availability for services
- Quarterly QC with DEB USA



Fasano G, Moffa F, Dechène J, Englert Y, Demeestere I. Vitrification of in vitro matured oocytes collected from antral follicles at the time of ovarian tissue cryopreservation. *Reprod Biol Endocrinol*. 2011 Nov 23;9:150.

Cobo A, Vajta G, Remohí J. Vitrification of human mature oocytes in clinical practice. *Reprod Biomed Online*. 2009;19 Suppl 4:4385.

Nagy ZP, Chang CC, Shapiro DB, Bernal DP, Kort HI, Vajta G. The efficacy and safety of human oocyte vitrification. *Semin Reprod Med*. 2009 Nov;27(6):450-5.

# Dedicated Fertility Preservation Teams at SJ and FAM



Many thanks to the entire Fertility Preservation teams at St. Jude Children's Research Hospital and Fertility Associates of Memphis



# Modify Protocols for Young Adolescent Cancer Patients

The Journal of  
**Obstetrics and  
Gynaecology**

**Journal of Obstetrics and Gynaecology**



ISSN: 0144-3615 (Print) 1364-6893 (Online) Journal homepage: <http://www.tandfonline.com/loi/ijog20>

## Ovulation induction and oocyte retrieval for fertility preservation in young adolescents newly diagnosed with medulloblastoma: a case series

William H. Kutteh, James L. Klosky, Daniel M. Green, Charlene K. Sparrow, Michael A. Kutteh, Giles W. Robinson & Amar Gajjar

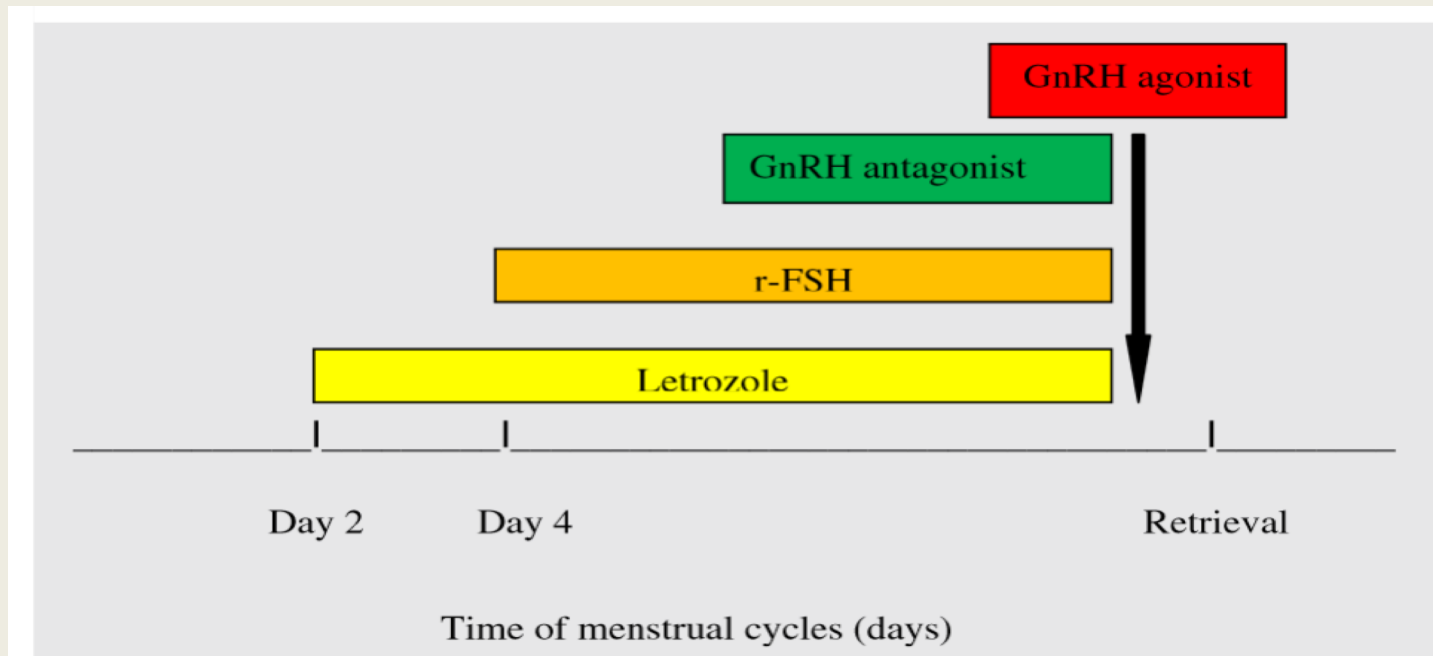
Successful oocyte retrieval if signs of puberty and one menses at age 12 and above.

Kutteh WH et al. J Obstet Gynaecol. 38:878-879, 2018

# Barriers to Fertility Preservation

## 4. PERCEIVED TREATMENT DELAY

- Oocytes can be preserved in as little as two weeks
- Protocols minimize estrogen levels and exposure



Reedy J, Oktay K. Ovarian stimulation and fertility preservation with the use of aromatase inhibitors in women with breast cancer. *Fertil Steril* 98:1363-9, 2012.

# Fertility Preservation Patient 14 yo with Medulloblastoma

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- 5/30/18- Fertility preservation referral, same day consult, medications ordered
- 6/1/18- Decision to start preservation, approval from oncology attending, started ovulation induction
- 6/12/18- Oocyte retrieval of 22 oocytes, 17 mature were frozen
- 6/18/18- Craniospinal radiation started
- 14 days from initial consult to freeze
- Delay in referral to FPC often 2 -6 weeks

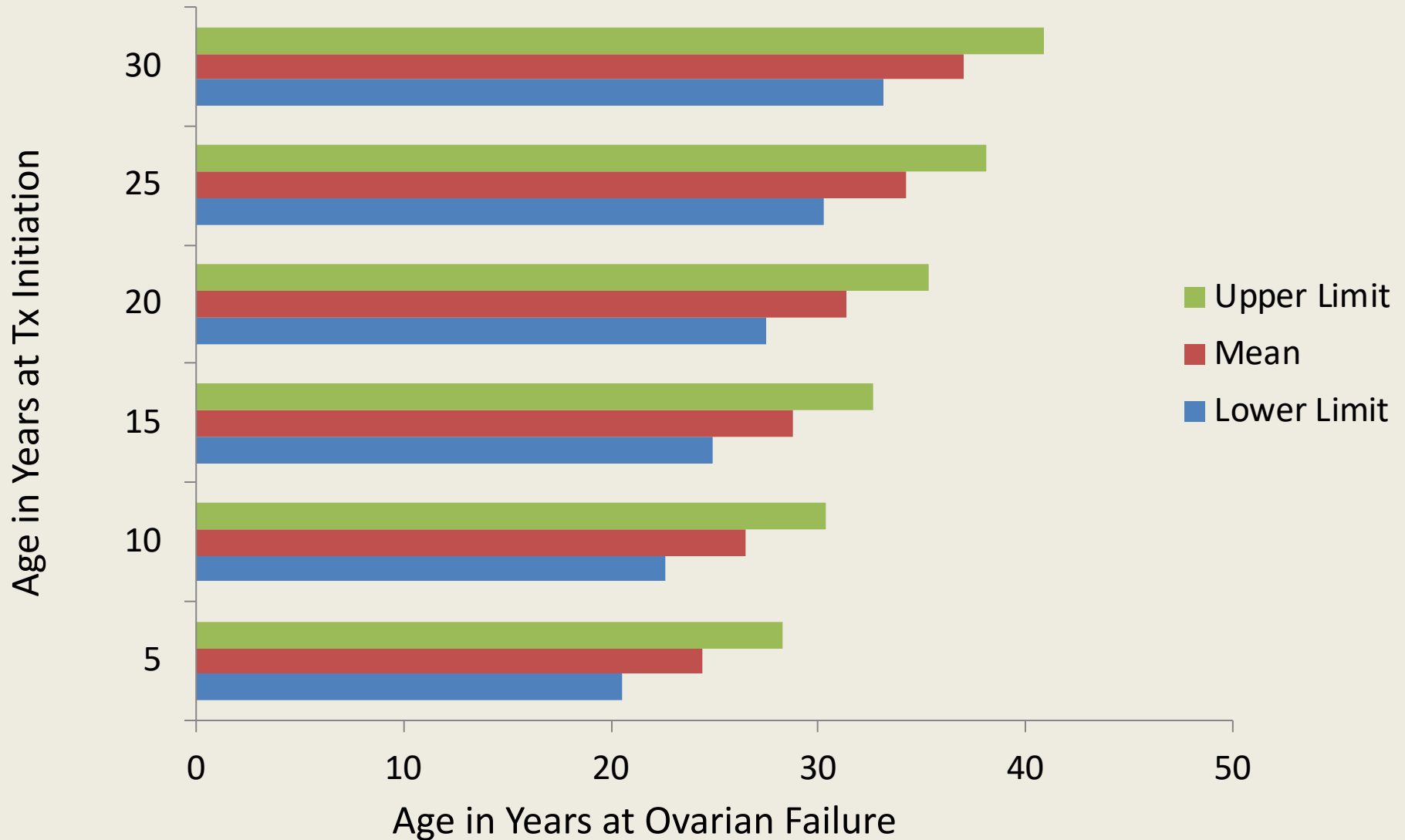
# SJ Patients who completed Cryopreservation with Fertility Associates of Memphis

	2012	2013	2014	2015	2016	2017	2018	2019 Projected
SPERM (# Patients)	6	11	15	23	25	16	22	23
EGGS (# Patients)	0	2	3	11	11	15	18	21



On-Site Fertility Preservation Clinic Initiated

# Predicted Age at Ovarian Failure after 6 Gy 95% Confidence Limits by Age at Treatment Initiation



# Oocyte Cryopreservation SJCRH

## Pre vs Post Therapy Results

	<b>Pre Therapy (n=29)</b>	<b>Survivors (n=47)</b>	<b>p Value (95 % CI)</b>
Age (years +/- SD) (range)	18.7 +/- 4.69 (13 -32)	18.0 +/- 3.94 (13-28)	0.556 (-3.56 to 1.96)
AMH (mg/ml +/- SD) (range)	5.92 +/- 4.61 (2.00 – 13.3)	2.20 +/- 1.71 (0.25 – 6.95)	<b>0.001</b> <b>(2.46 to 7.48)</b>
Days Stim to Cryo (range)	11.44 +/- 1.75 (9 – 15)	13.69 +/- 2.66 (9 -20)	<b>0.016</b> <b>(-4.05 to -0.45)</b>
# oocytes frozen (range)	20 +/- 4 (2 – 40)	14 +/- 10 (2 – 44)	0.090 (-1.23 to 16.03)

95% confidence interval of the difference between means

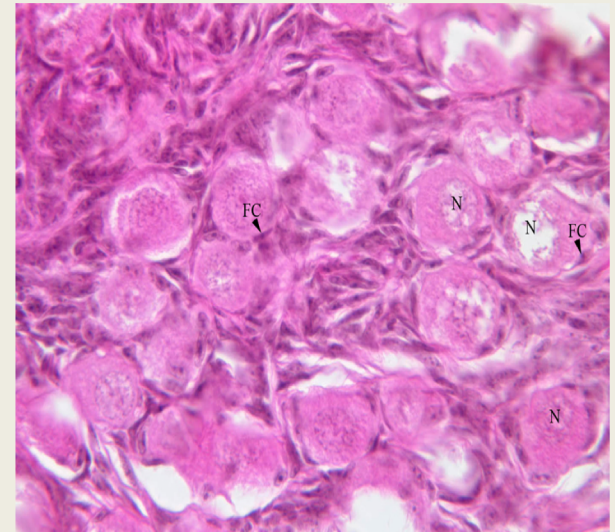


# Oocyte Cryopreservation SJCRH

## Preliminary Criteria for Success with Survivors

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- Resumption of some menstrual cycles
- AMH level of  $> 0.50$  ng/ml  
(best predictor of reserve)
- FSH level below 18 mIU/ml
- Antral follicle count of  $> 8$



All survivors meeting these criteria have  
successfully had oocytes frozen at SJCRH

# Barriers to Fertility Preservation

## 5. COST OF TREATMENT

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- National average cost of oocyte cryopreservation \$8,500 to \$11,000
- **SJCRH pays for oocyte cryopreservation and storage of oocytes up to 35 years of age**



# Active Research and Publishing



Fertilization: In Vitro

Brezina et al., J Fert In Vitro 2012, 2:6

<http://dx.doi.org/10.4172/2165-7491.1000e120>

Editorial

## The Impact of Elective Egg Freezing Technology

Paul R Brezina\*, Raymond W Ke, Jianchi Ding and William H Kutteh

*Coordinator of Reproductive Genetics, Fertility Associates of Memphis, Memphis, TN 38120, USA*

**Encouraged IVF Clinics to add this technology**

Brezina PR, Ke RW, Ding J, Kutteh WH. The Impact of Elective Egg Freezing Technology. J Fert In Vitro 2:6-8, 2012

## Lack of Specificity of Plasma Concentrations of Inhibin B and Follicle-Stimulating Hormone for Identification of Azoospermic Survivors of Childhood Cancer: A Report From the St Jude Lifetime Cohort Study

*Daniel M. Green, Liang Zhu, Nan Zhang, Charles A. Sklar, Raymond W. Ke, William H. Kutteh, James L. Klosky, Sheri L. Spunt, Monika L. Metzger, Fariba Navid, DeoKumar Srivastava, Leslie L. Robison, and Melissa M. Hudson*

Plasma markers do not predict future fertility in males

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# Cumulative alkylating agent exposure and semen parameters in adult survivors of childhood cancer: a report from the St Jude Lifetime Cohort Study



Daniel M Green, Wei Liu, William H Kutteh, Raymond W Ke, Kyla C Shelton, Charles A Sklar, Wassim Chemaitilly, Ching-Hon Pui, James L Klosky, Sheri L Spunt, Monika L Metzger, Deo Kumar Srivastava, Kirsten K Ness, Leslie L Robison, Melissa M Hudson

## Summary

**Background** Few data define the dose-specific relation between alkylating agent exposure and semen variables in adult survivors of childhood cancer. We undertook this study to test the hypothesis that increased exposure to alkylating Lancet Oncol 2014; 15: 1215-23  
Published Online

Impaired spermatogenesis was unlikely when the (CED) cyclophosphamide equivalent dose was less than 4000 mg/m<sup>2</sup>



ELSEVIER

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ADOLESCENT  
HEALTH

[www.jahonline.org](http://www.jahonline.org)

Original article

## Provider Influences on Sperm Banking Outcomes Among Adolescent Males Newly Diagnosed With Cancer



James L. Klosky, Ph.D.<sup>a,\*</sup>, L. Elizabeth Anderson<sup>b</sup>, Kathryn M. Russell, Ph.D.<sup>a</sup>, Lu Huang, M.S.<sup>c</sup>, Hui Zhang, Ph.D.<sup>c</sup>, Leslie R. Schover, Ph.D.<sup>d</sup>, Jessica L. Simmons, M.S.<sup>a</sup>, and William H. Kutteh, M.D., Ph.D.<sup>e,f</sup>

Provider training in communicating with adolescents and their families increased utilization of fertility preservation services.

## Effect of cranial irradiation on sperm concentration of adult survivors of childhood acute lymphoblastic leukemia: a report from the St. Jude Lifetime Cohort Study<sup>†</sup>

Daniel M. Green<sup>1,\*</sup>, Liang Zhu<sup>2,10</sup>, Mingjuan Wang<sup>2</sup>,  
Wassim Chemaitilly<sup>1,3</sup>, DeoKumar Srivastava<sup>2</sup>, William H. Kutteh<sup>4,5</sup>,  
Raymond W. Ke<sup>4,5</sup>, Charles A. Sklar<sup>6</sup>, Ching-Hon Pui<sup>7</sup>,  
Larry E. Kun<sup>8,11</sup>, Raul C. Ribeiro<sup>7</sup>, Leslie L. Robison<sup>1</sup>,  
and Melissa M. Hudson<sup>1,7,8,9</sup>

Cranial radiation therapy doses less than 26 Gy had no demonstrable adverse effect on sperm concentration or morphology

## Original Study

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# Parental Attitudes Toward Fertility Preservation in Female Adolescent Cancer Patients in Lebanon

Dalia Khalife MD<sup>1</sup>, William Kutteh MD, PhD, HCLD<sup>2</sup>, Hawraa Tarhini MD<sup>1</sup>, Ali Khalil MD<sup>1</sup>,  
Christine Beyrouthy MPH<sup>1</sup>, Ghina Ghazeeri MD<sup>1,\*</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, American University of Beirut Medical Center, Beirut, Lebanon

<sup>2</sup>Department of Reproductive Endocrinology, Vanderbilt University School of Medicine, Nashville, Tennessee

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Parents are not aware of the effect of cancer treatment on future fertility. Ethical, social, and religious barriers affect the decision making for fertility preservation.



# Gonadal Functioning and Perceptions of Infertility Risk Among Adult Survivors of Childhood Cancer: A Report From the St Jude Lifetime Cohort Study

Vicky Lehmann, PhD<sup>1</sup>; Wassim Chemaitilly, MD<sup>1</sup>; Lu Lu, MS<sup>1</sup>; Daniel M. Green, MD<sup>1</sup>; William H. Kutteh, MD, PhD<sup>1,2</sup>; Tara M. Brinkman, PhD<sup>1</sup>; Deo Kumar Srivastava, PhD<sup>1</sup>; Leslie L. Robison, PhD<sup>1</sup>; Melissa M. Hudson, MD<sup>1</sup>; and James L. Klosky, PhD<sup>1</sup>

Childfree survivors risk perceptions were discordant with laboratory-evaluated fertility status. Fertility related communication throughout survivorship is essential.

# Future Directions at St. Jude

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- Ovarian Tissue Cryopreservation offered but not paid for as still experimental
  - Prepubertal patients
  - Time constraints for oocyte cryopreservation
- Testicular Tissue Cryopreservation
  - Prepubertal patients
- Increase Fertility Consults for new patients
- AMH on all new female patients

Thank you



# Promise

WINTER 2015



**Preserving  
FERTILITY**  
New St. Jude clinic  
offers options *page 15*

Place of **REBIRTH**: After  
relapse, one child finds new  
life and health at St. Jude *page 2*

Revealing the **SECRETS** of  
a virulent flu strain *page 12*

