

Oncofertility Consortium

Fellow Education Day 2018

Please fill out the pre-course questionnaire!



Course objectives

- Describe currently available options for female and male fertility preservation including recent advances in embryo, oocyte, ovarian tissue, sperm, and testicular tissue cryopreservation.
- Formulate individualized treatment plans for patients throughout the reproductive spectrum who are interested in undergoing fertility preservation through cross-discipline collaboration.
- Appreciate the interdisciplinary approach necessary to achieve effective fertility preservation and survivorship care.

Schedule and format

Time	Topic	Speaker
08:00-08:15	Introduction to Course and Learning Teams	
08:15-09:00	Fertility Preservation in the Male	Jim Smith, MD, MS – Urologist and Director of Male Reproductive Health, University of California, San Francisco (UCSF)
09:05-9:15	Introduction to Team Based Learning	
09:20-10:20	Team based learning: Adult male and early reproductive female	Divya Shah, MD, MME – Reproductive Endocrinologist, University of Pennsylvania Wendy Vitek, MD – Reproductive Endocrinologist and Director of Fertility Preservation, University of Rochester
10:25-11:10	Fertility preservation in breast cancer patients: issues of timing	Jacqueline Jeruss, M.D., Ph.D. – Surgical Oncologist and Director, Breast Care Center, University of Michigan
11:15-12:15	<i>Lunch</i>	
12:20-01:05	Practical aspects of ovarian tissue cryopreservation in the pediatric population	Leslie Appiah, MD – Pediatric and Adolescent Gynecologist and Director of Oncofertility, Ohio State University/James Cancer Center
01:10-01:55	Team based learning: Late reproductive and pre-pubertal female	Divya Shah, MD, MME – Reproductive Endocrinologist and Infertility Specialist, University of Pennsylvania Wendy Vitek, MD – Reproductive Endocrinologist and Infertility Specialist, Director of Fertility Preservation, University of Rochester
02:00-03:00	Oncofertility State of the Union: advances from the past 5 years and projections for the next 5 years	Teresa Woodruff, PhD – Director Women's Health Research Institute, Chief, Division of Obstetrics and Gynecology-Fertility Preservation, Northwestern University

Team Introductions



Jim Smith, MD, MS



- Associate Professor,
Department of Urology
- Director of Male
Reproductive Health
- University of California,
San Francisco

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Team Based Learning

In-Class Activities (4 S's)

- **Significant Problems.** Teams work on a relevant, significant problem.
- **Same Problem.** Teams work on the same problem.
- **Specific Choice.** Teams required to make a specific choice.
- **Simultaneous Report.** Teams report simultaneously.



- High yield clinical scenarios in fertility preservation
- Not necessarily covered directly by lectures
- Multi-disciplinary focus
- Do not read ahead!

Clinical Case #1

Clinical Case

- A 17 year-old transwoman presents for fertility preservation. She recalls dressing up as a female as a child. In middle school, she started to feel like she wanted to change the way people referred to her gender, but "pushed that away and ignored it for a while." About two years ago, she started thinking again about wanting to change her body and her presentation. She started working with a therapist and has been treated for anxiety and depression with duloxetine. She has started presenting as female when she goes out socially. She is uncomfortable masturbating but will do so to facilitate tucking. She identifies as pansexual and has had oral and vaginal sex with male and female partners since age 15.
- She would like to be a mother in the future and would consider adoption. She is anxious to start gender affirming hormone therapy with spironolactone and estrace with the goals of having less body hair, body fat redistribution and breast development.

Question

- **How you would advise her regarding her fertility preservation options?**
 - A. Start gender affirming hormone therapy and revisit fertility when ready to conceive
 - B. Sperm bank via masturbation
 - C. Sperm bank via electroejaculation
 - D. Sperm bank via testicular sperm extraction
- **What factor(s) would you consider in making this decision?**

Question

- **Given the patient's age, which of the following steps should be taken?**
 - A. Obtain consent/assent from the patient for sperm banking
 - B. Obtain parental consent for sperm banking
 - C. Obtain parent consent for pornographic material in the collection room to assist with collection
 - D. Provide pornographic material from the collection room in the absence of parental consent
- **What factor(s) would you consider in making this decision?**

Question

- The sample revealed a total motile count of 2.1 million prior to cryopreservation with a post thaw total motile count of 0.1 million. She has 6 vials banked.
- **What are possible explanations for her severe oligospermia?**
 - A. Transwomen demonstrate higher incidence of oligospermia than cisgender sperm bankers
 - B. Nondisclosed hormone therapy
 - C. Altered testicular function related to tucking and tight clothes

Question

- She presents at age 27 with her partner who is a 25 year-old cis female. The patient is maintained on estrace 3 mg twice daily and spironolactone 100 mg twice daily. Her partner has regular cycles and has never tried to conceive. They would like to attempt insemination. Her labs reveal an estradiol of 154 pg/ml, free testosterone 1.28 ng/dl and total testosterone LC-MS/MS 61 ng/dl.
- **How would you counsel the couple regarding their options?**
 - A. Attempt collection for sperm cryopreservation
 - B. Stop estrace, spironolactone and tucking and attempt collection in 3 months
 - C. Pool the 6 banked vials for one insemination
 - D. Recommend donor sperm insemination
 - E. Recommend IVF/ICSI with cryopreserved sperm

Clinical Case #2

Clinical Case

- A 17 year old girl presents with recurrent Hodgkin's lymphoma. She is scheduled to undergo hematopoietic stem cell transplant. Her Oncology team has discussed the risk of subsequent infertility and would like to proceed with therapy as soon as possible. The patient has expressed interest in discussing fertility preservation. She underwent menarche at age 12 and has never been sexually active. She has regular cycles q 30 days and her LMP was three weeks ago.
- She has been seen and counseled with both parents presents and gives her assent for oocyte cryopreservation. A pelvic US performed at the time of initial consultation demonstrates a corpus luteal cyst on the right, an antral follicle count of 27, and a secretory endometrial lining of 11 mm. Labs are as follows: estradiol 135 pg/ml, LH 9.8 IU/L, progesterone 4.2 ng/ml.

Question

- **Given the patient's clinical presentation, which option(s) would you select for ovarian stimulation? What factor(s) would you consider in making this decision?**
 - A. Simultaneously starting gonadotropins and GnRH antagonist in the luteal phase.
 - B. Starting gonadotropins in the early follicular phase of the next menstrual cycle and adding a GnRH antagonist once the lead follicle reaches 12-14 mm.
 - C. Starting gonadotropins in the luteal phase and adding a GnRH antagonist once the lead follicle reaches 12-14 mm.
 - D. Administering a 3 day course of GnRH antagonist and awaiting a withdrawal bleed before starting gonadotropins.
 - E. Starting low dose leuprolide in the luteal phase and awaiting a withdrawal bleed before starting gonadotropins.

Question

Discuss advantages and disadvantages of each approach:

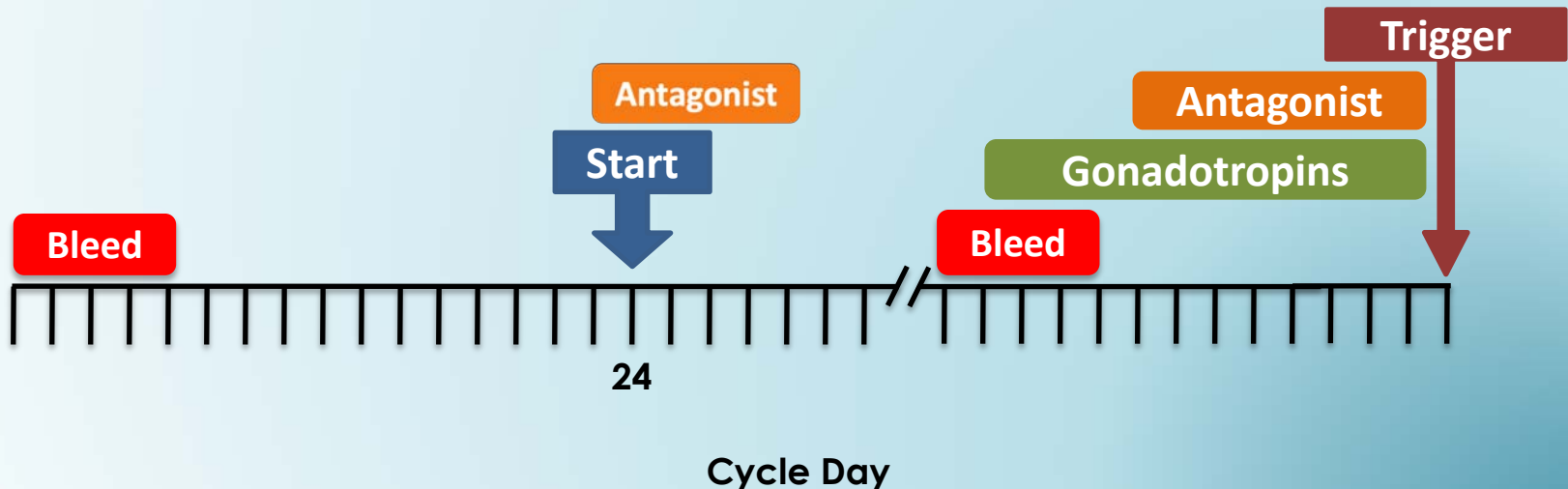
- A. Simultaneously starting gonadotropins and GnRH antagonist in the luteal phase.
- B. Starting gonadotropins in the early follicular phase of the next menstrual cycle and adding a GnRH antagonist once the lead follicle reaches 12-14 mm.
- C. Starting gonadotropins in the luteal phase and adding a GnRH antagonist once the lead follicle reaches 12-14 mm.
- D. Administering a 3-day course of GnRH antagonist and awaiting a withdrawal bleed before starting gonadotropins.
- E. Starting low dose leuprolide in the luteal phase and awaiting a withdrawal bleed before starting gonadotropins.

	A	B	C	D	E
Advantages					
Disadvantages					



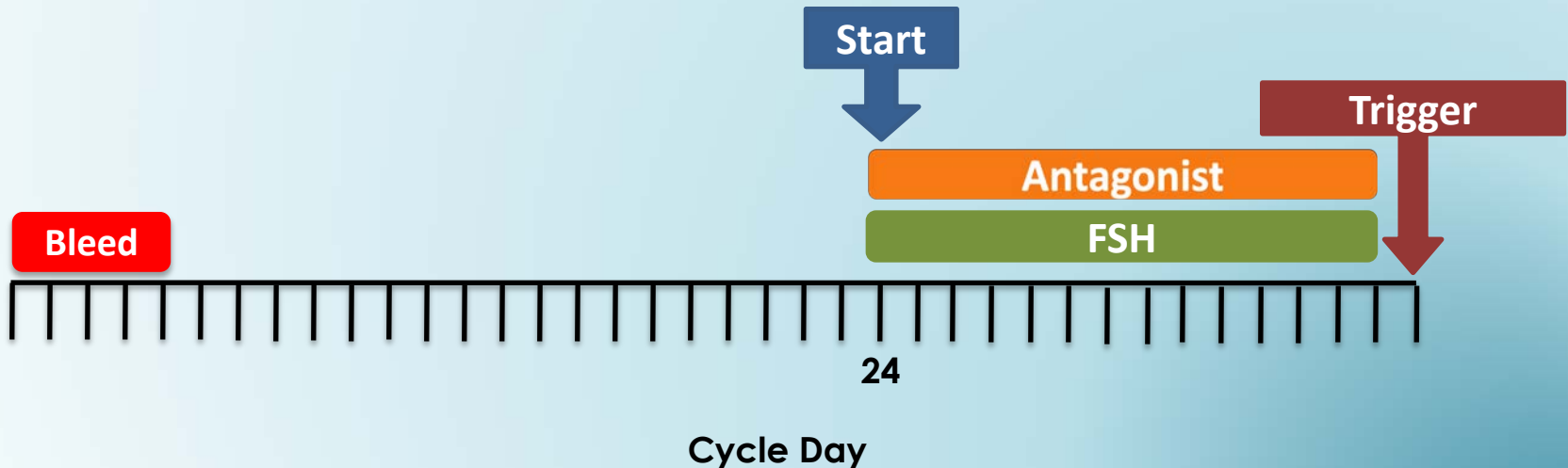
Luteolysis option #1

1. GnRH antagonist x 2-3 days in luteal phase.
2. Await bleed 2-4 days later.
3. Start gonadotropins on cycle day 2-3.
4. Add GnRH antagonist when lead follicle reaches 12-14 mm.
5. Trigger when lead follicles reach 18 mm.



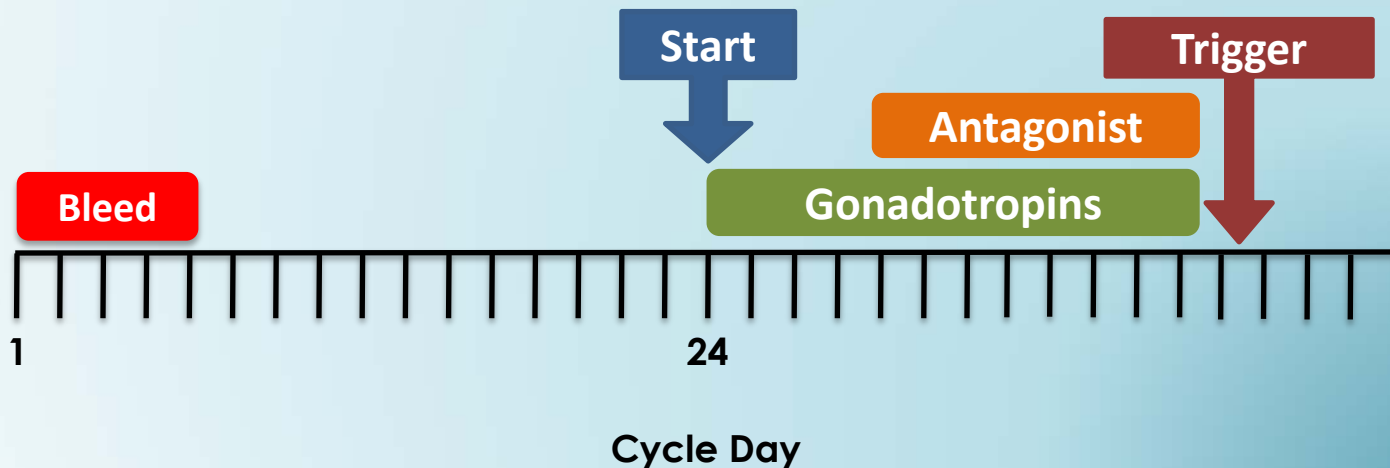
Luteolysis option #2

1. Start FSH and GnRH antagonist simultaneously in luteal phase.
2. FSH only for stimulation to avoid LH support of corpus luteum.
3. Trigger when lead follicles reach 18 mm.



Luteal phase: random start

1. Start gonadotropins in luteal phase.
2. Add GnRH antagonist when lead follicle reaches 12-14 mm.
3. Trigger when lead follicles reach 18 mm.



Question

- Suppose the same patient has US findings of a 19mm follicle on her right ovary and a 9 mm trilaminar endometrium at the time of presentation. Labs: estradiol 254 pg/ml, LH 13.4 IU/L, progesterone 1.3 ng/ml.

How would this change your approach to ovarian stimulation?

- A. Await menses before starting gonadotropins in the early follicular phase. Add a GnRH antagonist once the lead follicle reaches 12-14 mm.
- B. Start gonadotropins in the late follicular phase regardless of the presence of a dominant follicle. Add a GnRH antagonist once another lead follicle reaches 12-14 mm.
- C. Await ovulation before starting low dose leuprolide in the luteal phase. Await withdrawal bleed before starting gonadotropins.
- D. Monitor for a dominant follicle and trigger ovulation with HCG before starting gonadotropin stimulation. Add a GnRH antagonist once a lead follicle reaches 12-14 mm.
- E. Await ovulation before initiating one of the luteolytic stimulation options presented above.

Question

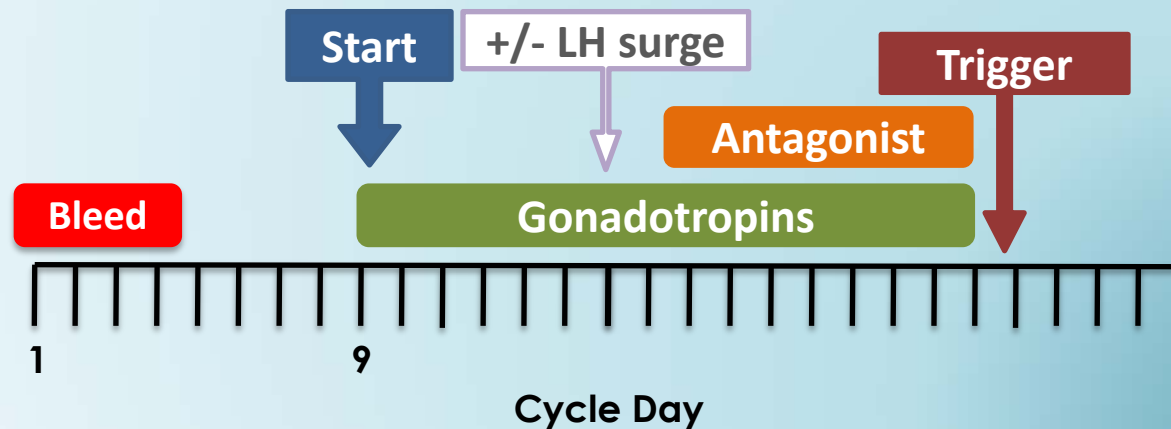
Discuss advantages and disadvantages of each approach:

- A. Await menses before starting gonadotropins in the early follicular phase. Add a GnRH antagonist once the lead follicle reaches 12-14 mm.
- B. Start gonadotropins in the late follicular phase regardless of the presence of a dominant follicle. Add a GnRH antagonist once another lead follicle reaches 12-14 mm.
- C. Await ovulation before starting low dose leuprolide in the luteal phase. Await withdrawal bleed before starting gonadotropins.
- D. Monitor for a dominant follicle and trigger ovulation with HCG before starting gonadotropin stimulation. Add a GnRH antagonist once a lead follicle reaches 12-14 mm.
- E. Await ovulation before initiating one of the luteolytic stimulation options presented above.

	A	B	C	D	E
Advantages					
Disadvantages					

Late follicular phase: random start option #1

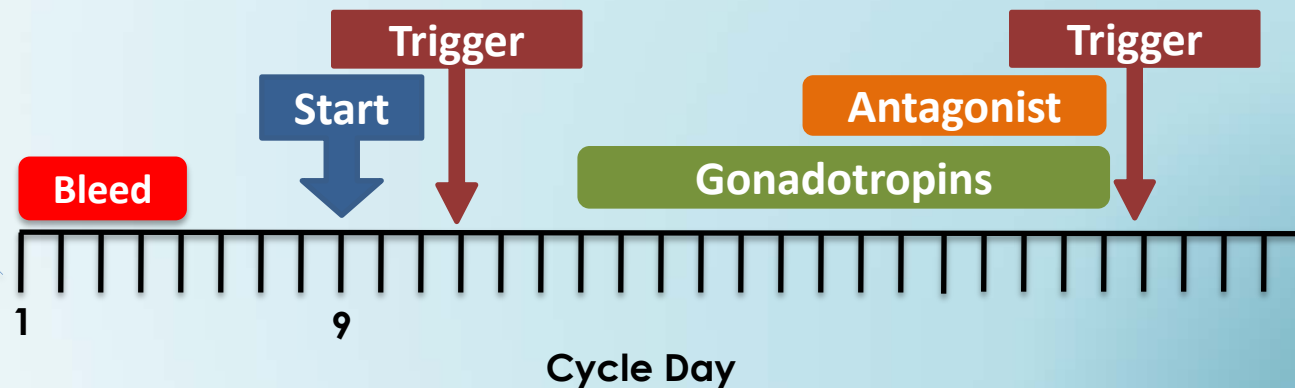
1. Start gonadotropins on day of presentation.
2. Add GnRH antagonist when secondary cohort following lead follicle reaches 12 mm regardless of size of dominant follicle.
3. Disregard any spontaneous LH surge.
4. Trigger when lead follicles in secondary cohort reach 18 mm.





Late follicular phase: random start option #2

1. Trigger ovulation when dominant follicle reaches 18 mm.
2. Start gonadotropins 2-3 days after trigger.
3. Add GnRH antagonist when lead follicle reaches 12-14 mm.
4. Trigger when lead follicles reach 18 mm.



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Jacqui Jeruss, MD, PhD



- Associate Professor, Departments of Surgery, Pathology, and Biomedical Engineering, University of Michigan
- Director, Breast Care Center
- Director, Breast Surgical Oncology Fellowship

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Leslie Appiah, MD



- Associate Professor,
Pediatric and Adolescent
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- The Ohio State
University/James Cancer
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Clinical Case #3

Clinical Case

- A 38 year-old Go palpated a left breast mass. Mammography revealed a 2-cm spiculated mass and ultrasound guided needle biopsy was performed. Pathology revealed an invasive ductal carcinoma that was ER/PR positive and HER-2/neu negative.
- Given a strong family history of breast cancer, she underwent genetic testing and was found to carry a *BCRA* mutation. She underwent a left modified radical mastectomy (positive lymph nodes) and right prophylactic mastectomy with immediate reconstruction. She was diagnosed with clinical Stage IIB breast cancer.
- Adjuvant chemotherapy with adriamycin and cyclophosphamide followed by paclitaxel for 4 cycles has been recommended. She will also receive radiation therapy to the left axilla and hormone therapy with Tamoxifen for at least 5 years. She has been counseled regarding bilateral salpingo-oophorectomy at the completion of child bearing. She presents to discuss fertility preservation. She is in a committed relationship but is not married.

Question

- **Given the patient's clinical presentation, which option(s) would you select for fertility preservation and why?**
 - A. Immediate controlled ovarian stimulation with subsequent oocyte cryopreservation
 - B. Immediate controlled ovarian stimulation with subsequent embryo cryopreservation
 - C. Immediate controlled ovarian stimulation with subsequent embryo cryopreservation with preimplantation genetic diagnosis (PGD) for *BRCA* mutation
 - D. Ovarian tissue cryopreservation with bilateral salpingo-oophorectomy
 - E. Leuprolide (Lupron) prior to and during chemotherapy
- **What factor(s) would you consider in making this decision?**

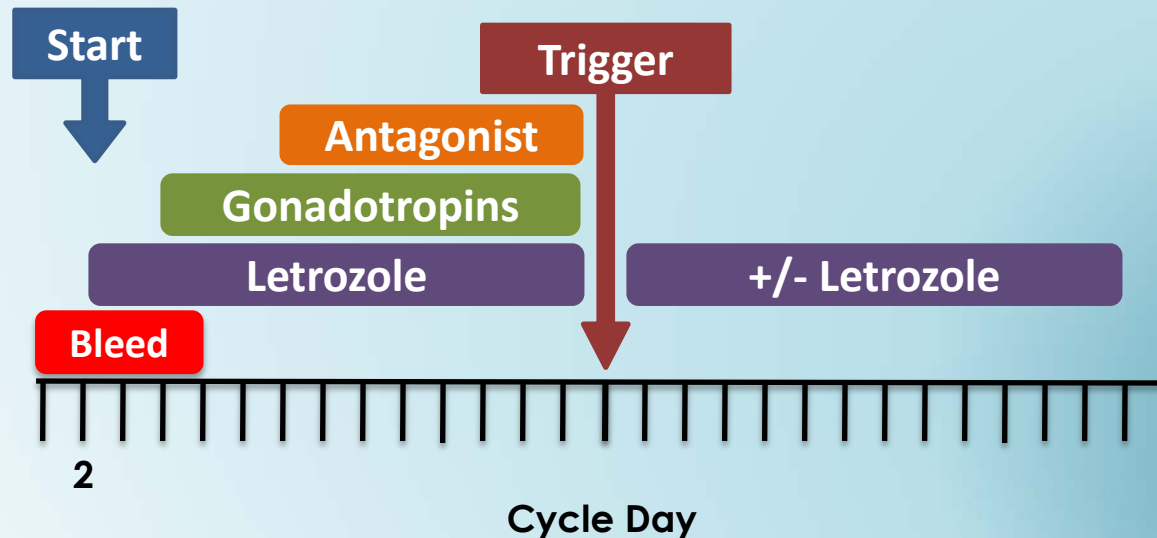
Question

- **If you advised immediate controlled stimulation and the patient is her early follicular phase, which option(s) would you select for ovarian hyperstimulation and why?**
 - A. Starting gonadotropins in the early follicular phase and add a GnRH antagonist once the lead follicle reaches 12-14 mm
 - B. Starting letrozole on the second day of the menstrual cycle and continue until trigger, add gonadotropin 2 days after letrozole initiation, trigger with HCG once 2 follicles reach 19-20 mm
 - C. Starting letrozole on the second day of the menstrual cycle and continue until trigger, add gonadotropin 2 days after letrozole initiation, trigger with luprolide acetate once 2 follicles reach 19-20 mm
 - D. Start or restart letrozole for 5-7 days post retrieval or until the estradiol level is <50 pg/ml
- **What factor(s) would you consider in making this decision?**

Stimulation for estrogen-sensitive tumors: letrozole



1. Start letrozole on cycle day 2-3.
2. Start gonadotropins 2 days later.
3. Add GnRH antagonist when lead follicle reaches 12-14 mm.
4. Trigger when lead follicles reach 19-20 mm.
5. Restart letrozole after retrieval and continue until estradiol <50 pg/mL.



Question

- She presents for follow up 2 years later and appears to be disease free. She is taking Tamoxifen daily. She and her partner recently married. They are ready to start a family.
- **Which option(s) would you select for pregnancy and why?**
 - A. Discontinuation of Tamoxifen for two months prior to attempting a pregnancy and plan to restart Tamoxifen after pregnancy
 - B. Continue Tamoxifen for 3 more years and attempt pregnancy at the completion of her hormone therapy
 - C. Continue Tamoxifen for 3 more years and recommend gestational carrier
 - D. Perform a natural cycle frozen embryo transfer
 - E. Perform a medicated or programmed frozen embryo transfer
- **What factor(s) would you consider in making this decision?**

Clinical Case #4

Clinical Case

- A 12-year-old girl presents with diplopia and is found to have a pineal tumor (primitive neuroectodermal tumor or PNET) on head CT. She underwent craniotomy two weeks ago. Her subsequent treatment plan includes craniospinal radiation therapy with proton beam and cyclophosphamide chemotherapy. Her Oncology team requests a consultation for fertility preservation.
- She presents with her mother. She is premenarchal and has not yet experienced breast development. She has no other past medical or past surgical history other than what is described above. Her medications include amlodipine and marinol. She has never been sexually active.

Question

- **Given the patient's clinical presentation, Which option(s) would you select for fertility preservation and why?**
 - A. Immediate controlled ovarian stimulation with subsequent oocyte cryopreservation
 - B. Laparoscopic ovarian transposition
 - C. Ovarian tissue cryopreservation
 - D. Laparoscopic ovarian transposition with concurrent ovarian tissue cryopreservation
- **What factor(s) would you consider in making this decision?**

Question

- If the patient was undergoing radiation therapy with traditional x-ray, would this change your decision? Which option would you select for fertility preservation and why?
 - A. Immediate controlled ovarian stimulation with subsequent oocyte cryopreservation
 - B. Laparoscopic ovarian transposition
 - C. Ovarian tissue cryopreservation
 - D. Laparoscopic ovarian transposition with concurrent ovarian tissue cryopreservation

Question

- If you advised ovarian transposition, how would you perform the procedure? Why?
 - A. Cut utero-ovarian ligament, transfix ovary inferomedially to uterosacral ligament
 - B. Cut utero-ovarian ligament and fallopian tube, transfix ovary to lateral pelvic sidewall above level of ischial spines
 - C. Cut utero-ovarian ligament and fallopian tube, tunnel ovary through peritoneal window and transfix to lateral pelvic sidewall above level of ischial spines

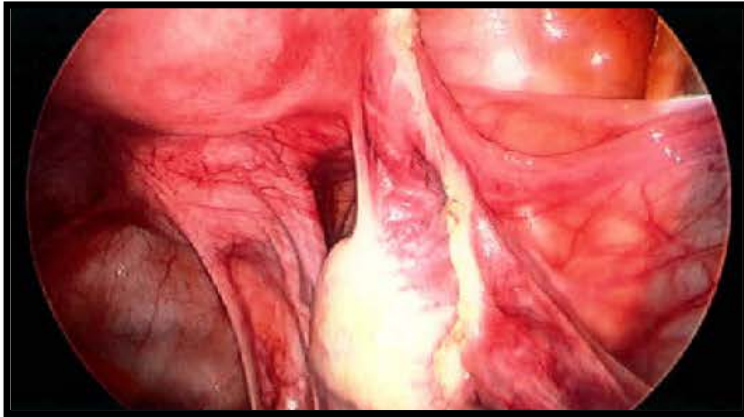
Question

- Suppose the patient was undergoing pelvic radiation therapy for localized rectal cancer.
- **Which option(s) would you select for fertility preservation and why?**
 - A. Immediate controlled ovarian stimulation with subsequent oocyte cryopreservation
 - B. Laparoscopic ovarian transposition
 - C. Ovarian tissue cryopreservation
 - D. Laparoscopic ovarian transposition with concurrent ovarian tissue cryopreservation
- **What factor(s) would you consider in making this decision?**

Question

- **How would you now perform the ovarian transposition procedure and why?**
 - A. Cut utero-ovarian ligament, transfix ovary inferomedially to uterosacral ligament
 - B. Cut utero-ovarian ligament and fallopian tube, transfix ovary to lateral pelvic sidewall above level of ischial spines
 - C. Cut utero-ovarian ligament and fallopian tube, tunnel ovary through peritoneal window and transfix to lateral pelvic sidewall above level of ischial spines
- **What factor(s) would you consider in making this decision?**

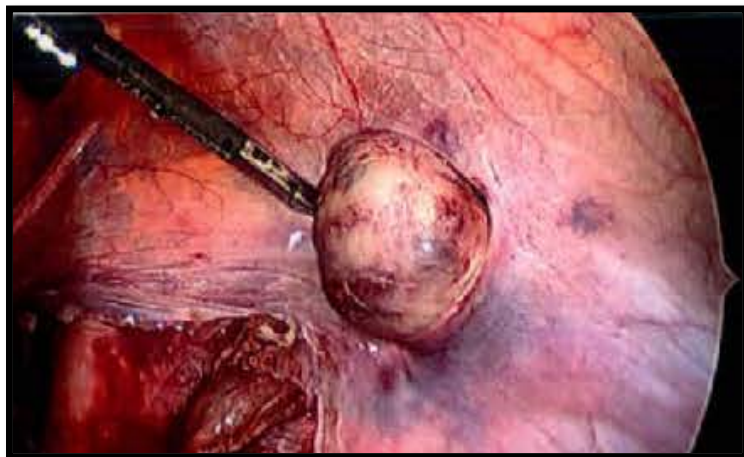
Surgical technique



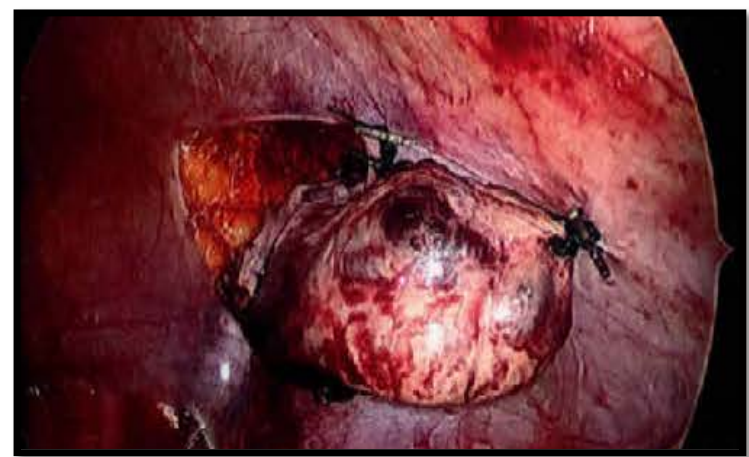
Select ovary for transposition



Free utero-ovarian ligament and skeletonize IP



Peritoneal window above level of field



Ovary sutured and clips applied

Question

- Suppose the patient described above initially presented with leukemia. Her oncology team plans induction chemotherapy in the near future and has counseled her that there is a high likelihood of her requiring a future hematopoietic stem cell transplant.
- **Which option would you select for fertility preservation and why?**
 - A. Immediate controlled ovarian stimulation with subsequent oocyte cryopreservation
 - B. Laparoscopic ovarian transposition
 - C. Ovarian tissue cryopreservation
 - D. Laparoscopic ovarian transposition with concurrent ovarian tissue cryopreservation
 - E. None of the above
- **What factor(s) would you consider in making this decision?**

Question

- **If you advised ovarian tissue cryopreservation, when would you advise the patient to undergo this procedure and why?**
 - A. Before induction chemotherapy
 - B. After induction chemotherapy but before hematopoietic stem cell transplant
 - C. After hematopoietic stem cell transplant
- **What factor(s) would you consider in making this decision?**

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Teresa Woodruff, PhD



- Director, Women's Health Research Institute
- Chief, Reproductive Biology Research, Department of Obstetrics and Gynecology
- Thomas J. Watkins
Memorial Professor of
Obstetrics and Gynecology

Appreciation



ASRM air learning certificate course



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[Home](#) / [MD120: Principles of Fertility Preservation for Re...](#) / **Enrollment options**

MD120: Principles of Fertility Preservation for Reproductive Health Providers Certificate Course

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- ▼ Current course
 - ▼ **MD120: Principles of Fertility Preservation for Re...**
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MD120: Principles of Fertility Preservation for Reproductive Health Providers Certificate Course

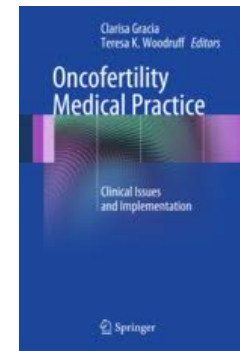
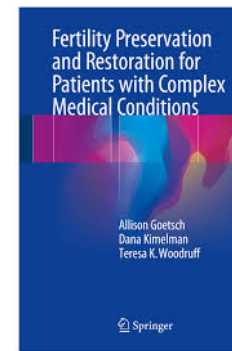
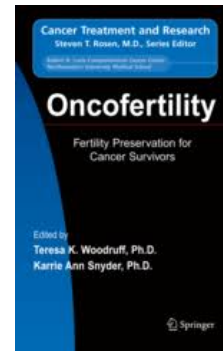
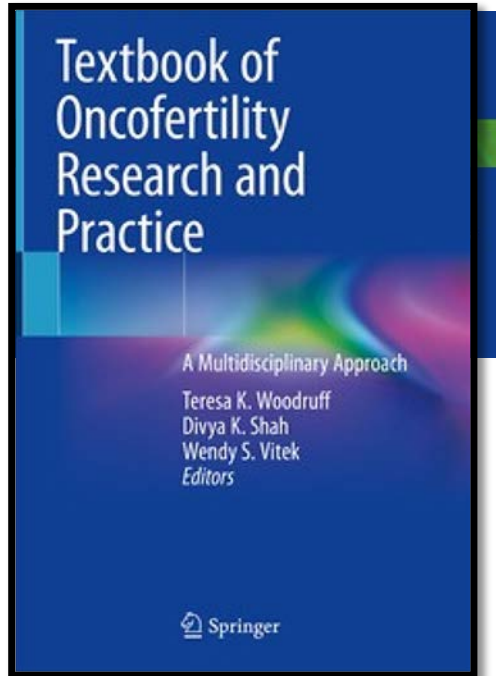
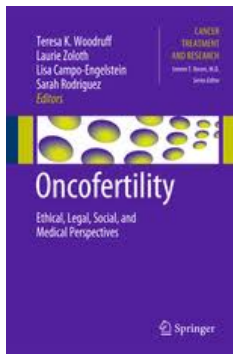
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Please fill out the post-course questionnaire and evaluation!



QUESTIONNAIRE

Very often

Sometimes

Always

