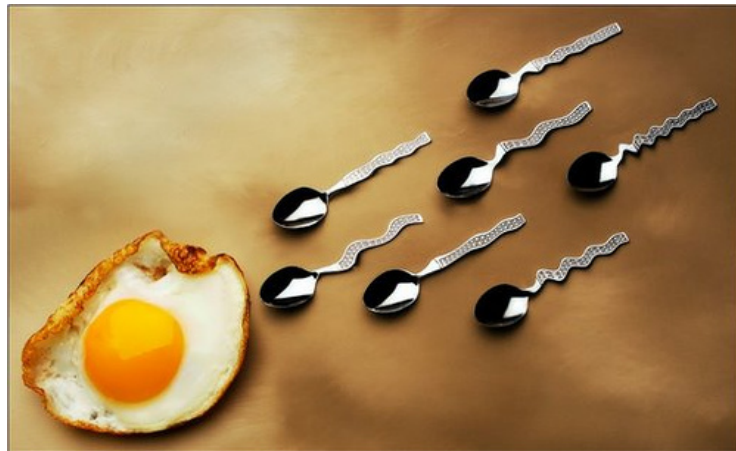


Cancer and Fertility

**Joanne Frankel Kelvin, MSN, RN, AOCN
Clinical Nurse Specialist
Memorial Sloan-Kettering Cancer Center**



Advances in cancer treatment have led to improvements in survival

Survival rates

Adult cancers 68%

Pediatric cancers 83%

~13.7 million cancer survivors in the US

5% are younger than 40 years of age

	0–9	10–19	20–29	30–39
Male	18,499	43,137	74,785	134,634
Female	8,636	36,912	105,114	250,921

Siegel 2012, De Moor 2013

Cancer treatments affect fertility

Surgery

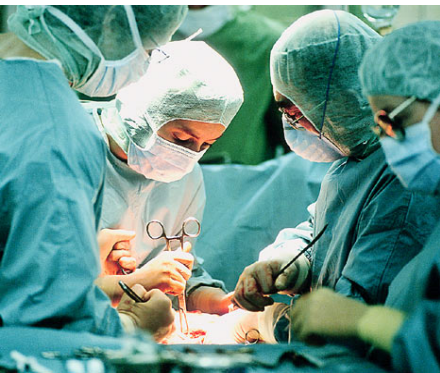
- If reproductive structures removed/altered

Radiation Therapy

- Based on field of treatment and dose

Chemotherapy and Hormonal Therapy

- Based on agent and dose



Patient factors also affect fertility

- ▶ Age (females)
- ▶ Diagnosis
- ▶ Obesity
- ▶ Tobacco smoking, alcohol, drugs
- ▶ Pre-treatment fertility

Fertility is an important issue for cancer survivors

Many young cancer patients...

- ▶ Have not yet started or completed their families at the time of diagnosis
- ▶ Want to be parents after treatment
- ▶ Do not recall being told of risk of infertility
- ▶ Are distressed or concerned about possibility of infertility

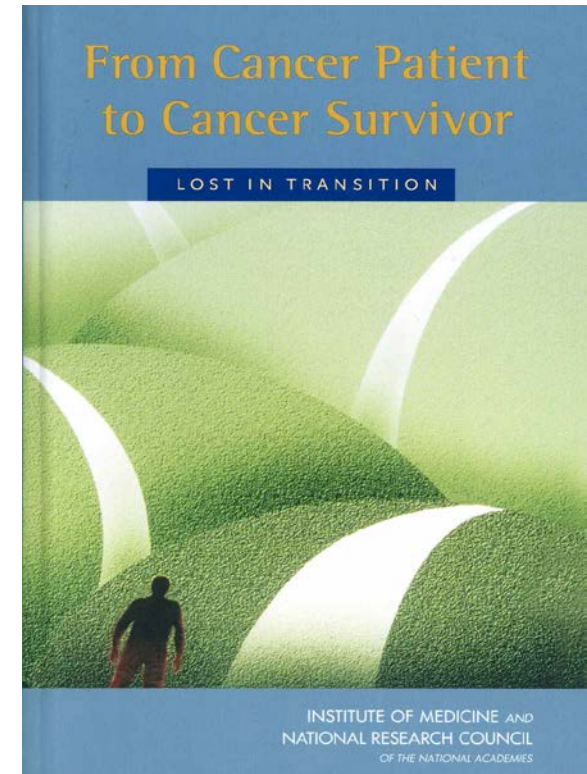
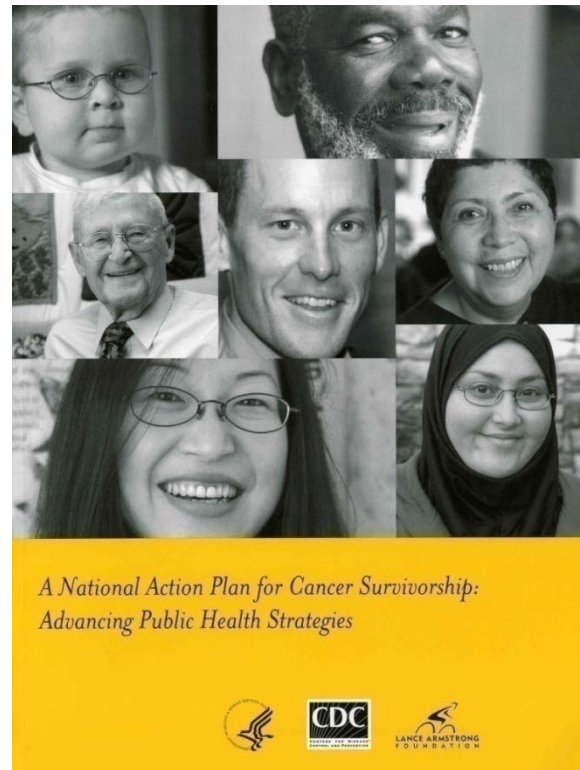
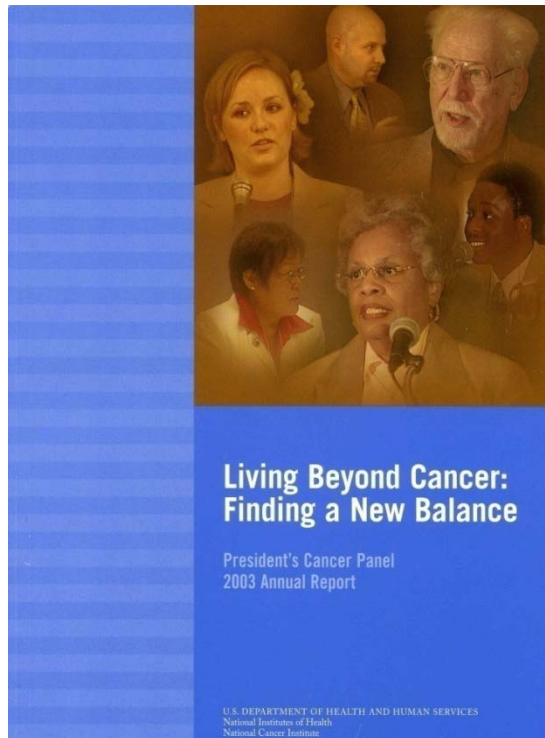
Crawshaw, et al, 2009; Duffy, et al, 2005; Partridge, et al, 2004; Peate, et al, 2009; Schover, et al, 1999; Schover, et al, 2002; Schover, 2005; Schover, et al, 2002; Thewes, et al, 2005; Tschudin & Bitzer, 2009; Wenzel, et al, 2005

Clinicians don't always discuss fertility with their patients

- ▶ Believe this is important
- ▶ Inadequate knowledge
- ▶ Barriers
 - Lack of time
 - Lack of resources
 - Concern about cost
 - Don't know where to refer

King, et al, 2008; Kotronoulas, Papadopoulou, & Patiraki, 2009; Quinn, et al, 2007; Quinn, et al, 2009; Schover, et al, 2002; Vadaparampil, et al, 2007

There is national recognition of the need to address fertility concerns



There is professional recognition of the need to address fertility concerns

Health care providers have a responsibility to

- Inform patients about the risks that their cancer treatment will permanently impair fertility
- Discuss options for fertility preservation and parenting after cancer
- Refer to appropriate specialists

American Society of Clinical Oncology (Loren et al, 2013)

American Medical Association (2013)

NCCN AYA Adolescent and Young Adult Clinical Oncology Guidelines (NCCN, 2012)

European Society for Medical Oncology (Pentheroudakis et al, 2010)

American Academy of Pediatrics (Fallat et al, 2008)

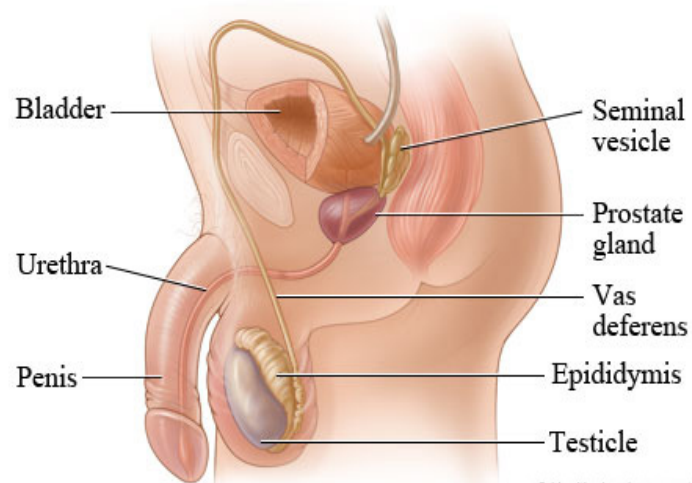
American Society of Reproductive Medicine (ASRM, 2005)

Outline

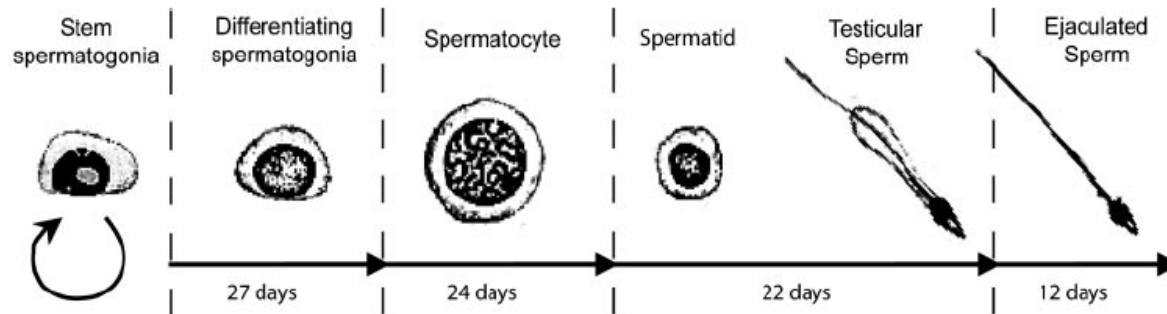
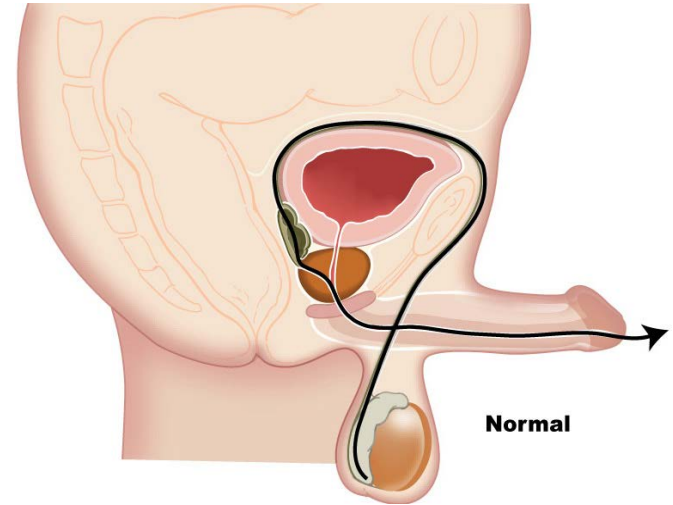
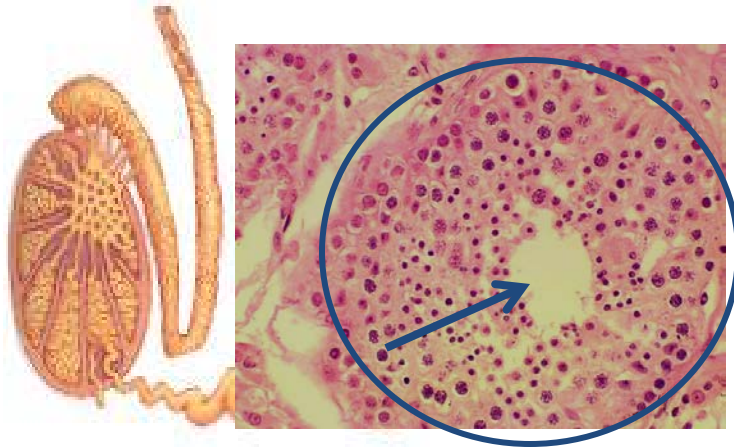
- ▶ Basics of reproductive biology
- ▶ Effects of treatment on fertility
- ▶ Options for fertility preservation
- ▶ Resources at MSKCC to help you discuss fertility with your patients

MALES

Basics of Reproductive Biology Effects of Treatment on Fertility Options for Fertility Preservation



Spermatogenesis and Ejaculation



Fertility Effects of Treatment

Impaired sperm production

- ▶ Depletion of stem cells and developing sperm
Recovery – Oligospermia – Azoospermia

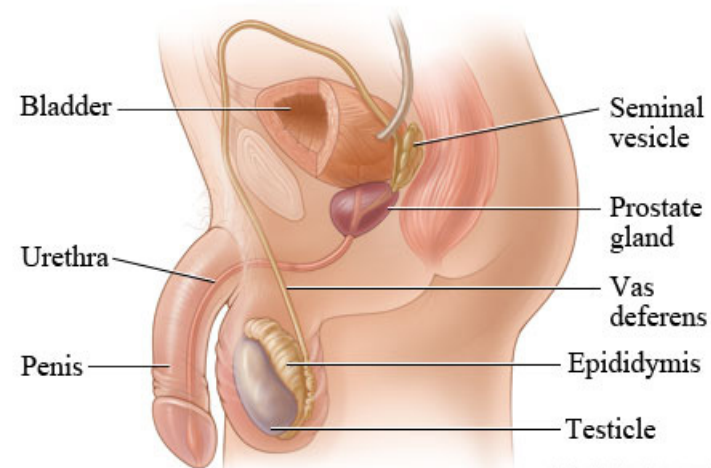


Impaired sperm transport

- ▶ Injury to pelvic ducts/blood vessels/nerves →
erectile/ejaculatory dysfunction

Pituitary gland dysfunction

- ▶ Disruption of hypothalamic-pituitary-gonadal axis



Evaluation of Male Fertility

It is impossible to predict with certainty who will be affected permanently

▶ Semen analysis (WHO criteria, 2010)

- Volume 1.5 (1.4–1.7) ml
- Sperm concentration 15 (12–16) million/ml
- Progressive motility 32 (31–34)%
- Vitality 58 (55–63)%

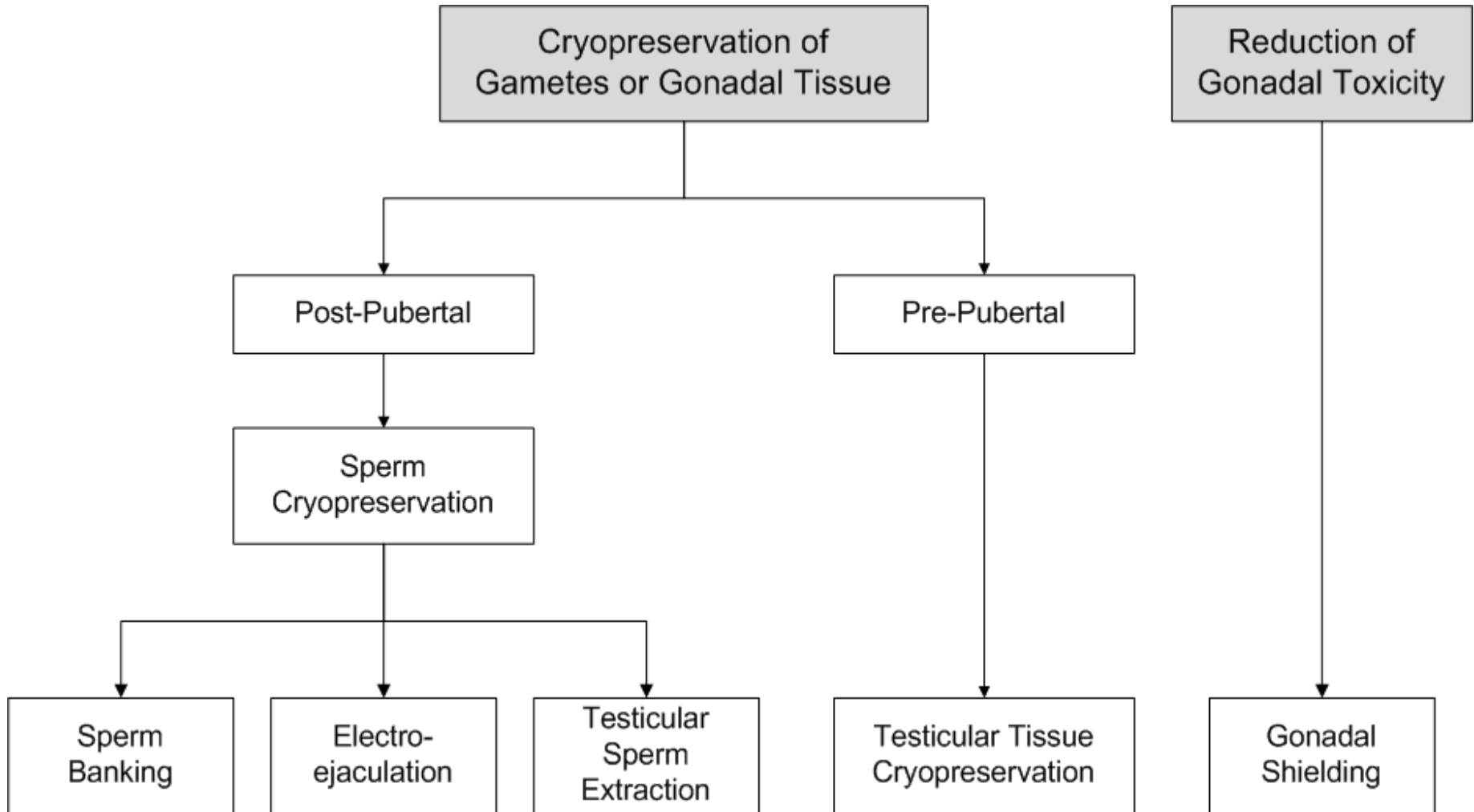
DNA integrity testing not included

▶ Hormonal analysis

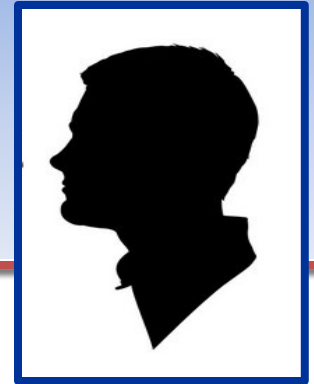
- FSH, LH, Testosterone

Males

Fertility Preservation Options



John



19 year old male

- ▶ Diagnosis: Testicular cancer
- ▶ Treatment plan: Orchiectomy followed by chemotherapy with BEP (bleomycin, etoposide, cisplatin)
- ▶ Social: single college student, no children

What is available for this patient?

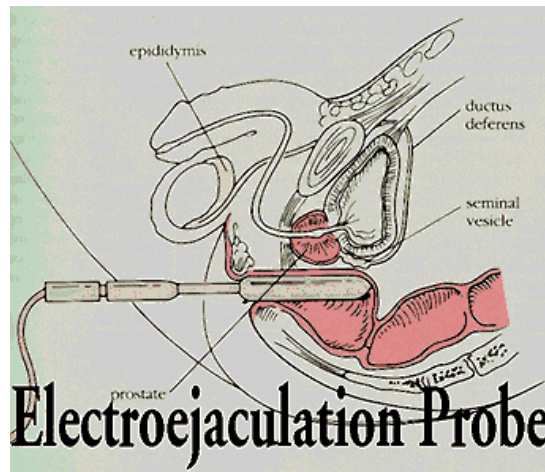
Sperm Cryopreservation (Banking)

Semen collected, analyzed, placed in vials, frozen, and stored for possible future use

Sperm Bank Collection

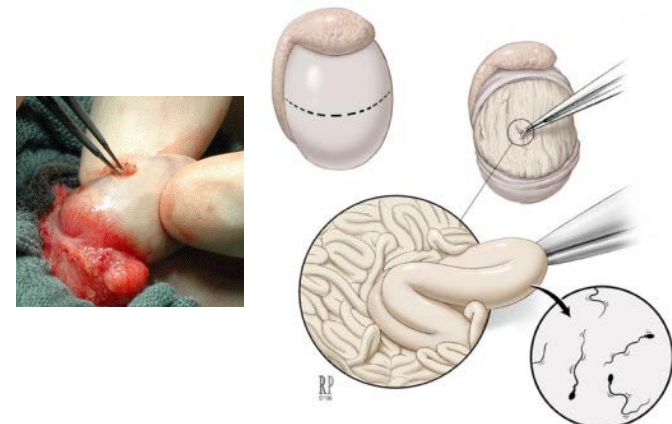
Manual stimulation
3 collections
Abstain 2-5 days

Electroejaculation EEJ



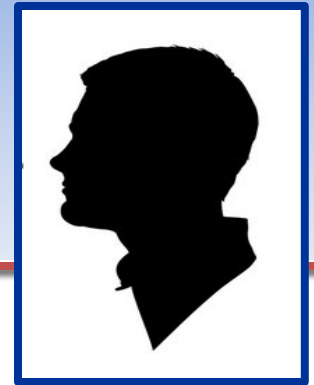
If patient is unable to collect manually

Testicular Sperm Extraction TESE



If patient is azoospermic

Peter



8 year old male

- ▶ Diagnosis: Rhabdomyosarcoma
- ▶ Treatment plan: Chemotherapy with VAC (vincristine, doxorubicin, cyclophosphamide)
- ▶ Social: school-aged child

What is available for this patient?

Testicular Tissue Cryopreservation

- ▶ Tissue biopsied, frozen, and stored for potential future use
 - Tissue reimplantation – no live births to date
Concern about re-implanting cancer cells
 - In vitro maturation – no live births to date
- ▶ Investigational

Sam



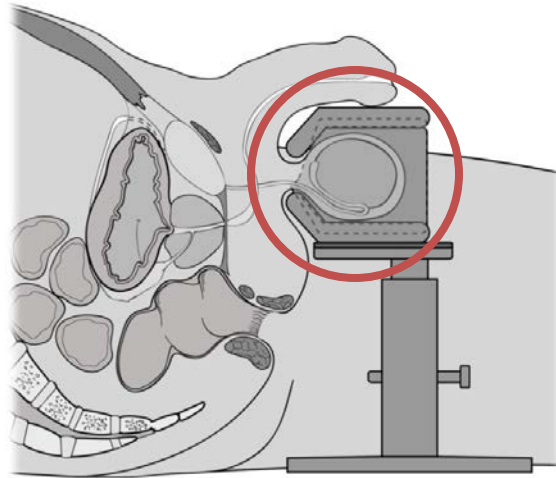
38 year old male

- ▶ Diagnosis: Rectal cancer
- ▶ Treatment plan: Pelvic RT with CI fluorouracil followed by surgical resection and adjuvant chemotherapy with FOLFOX (fluorouracil and oxaliplatin)
- ▶ Social: married with 3 year old son

What is available for this patient?

Gonadal Shielding

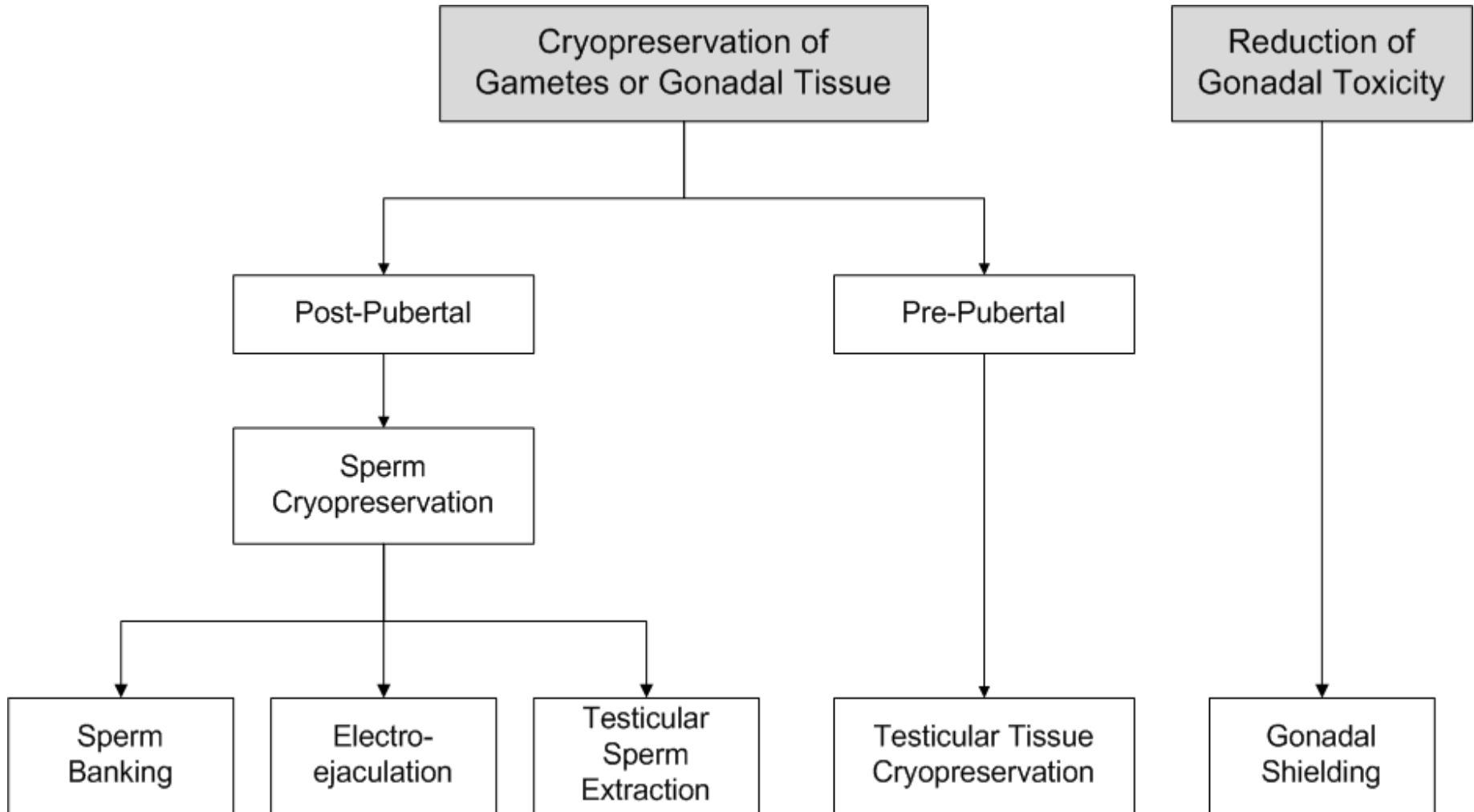
During pelvic/inguinal field radiation



- ▶ With IMRT to minimize testicular dose
- ▶ Also recommend sperm banking before treatment

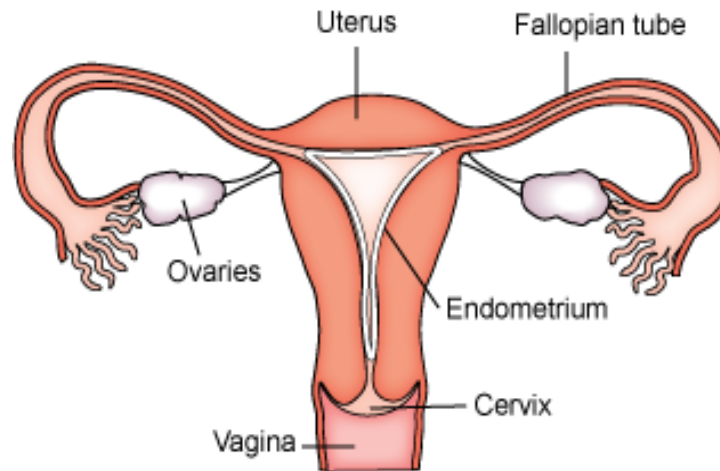
Males

Fertility Preservation Options

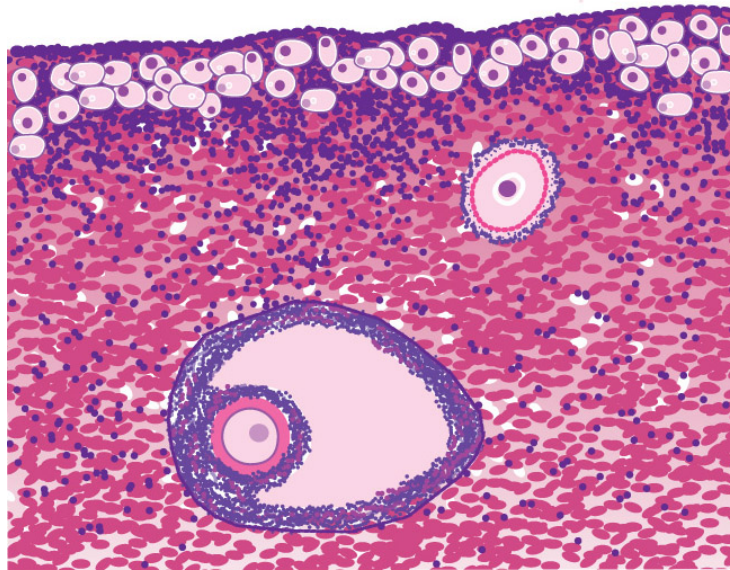


FEMALES

Basics of Reproductive Biology Effects of Treatment on Fertility Options for Fertility Preservation

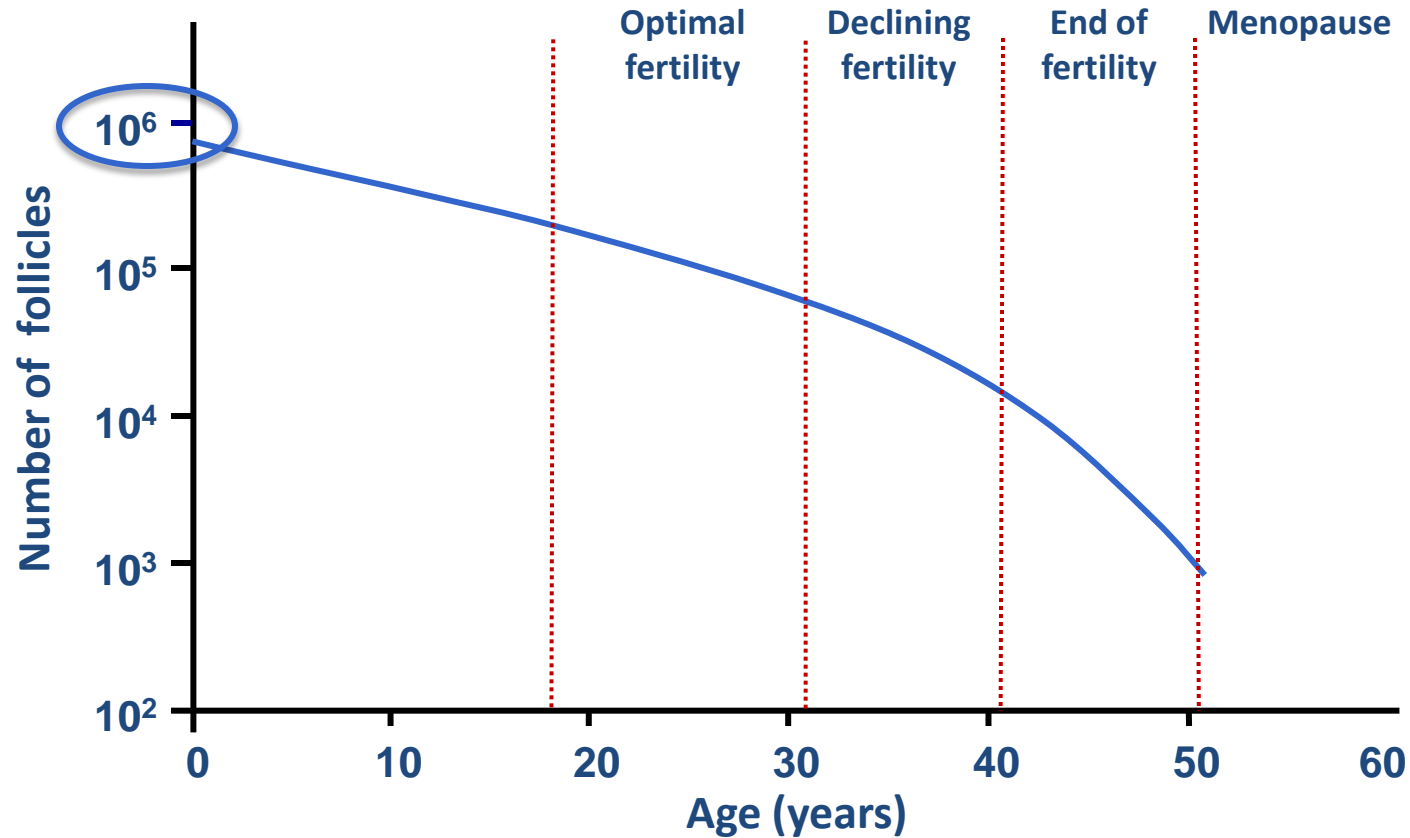


Ovarian Cortex



Ovarian Reserve = number and quality of eggs

Effect of Age on Ovarian Reserve



Loss of follicles → Infertility, Menopause

Females

Fertility Effects of Treatment

Depletion of ovarian follicle pool (oocytes)

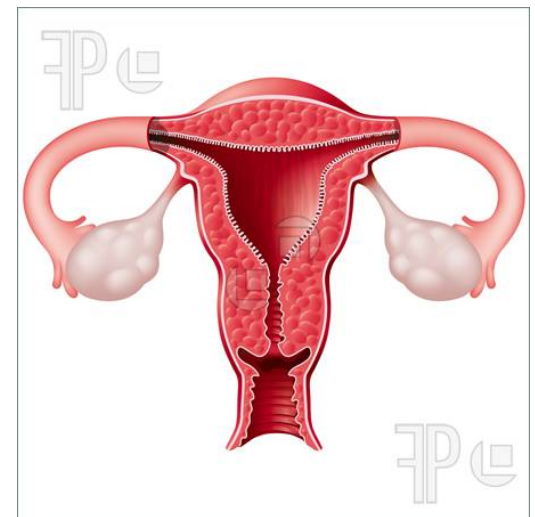
- ▶ Premature ovarian failure → infertility, menopause
May have narrowed window of reproductive opportunity

Pituitary gland dysfunction

- ▶ Disruption of hypothalamic-pituitary-gonadal axis

Uterine damage

- ▶ Vascular changes, endometrial injury → inability to support embryo implantation
- ▶ Myometrial fibrosis → inability to accommodate a growing fetus



Evaluation of Female Fertility

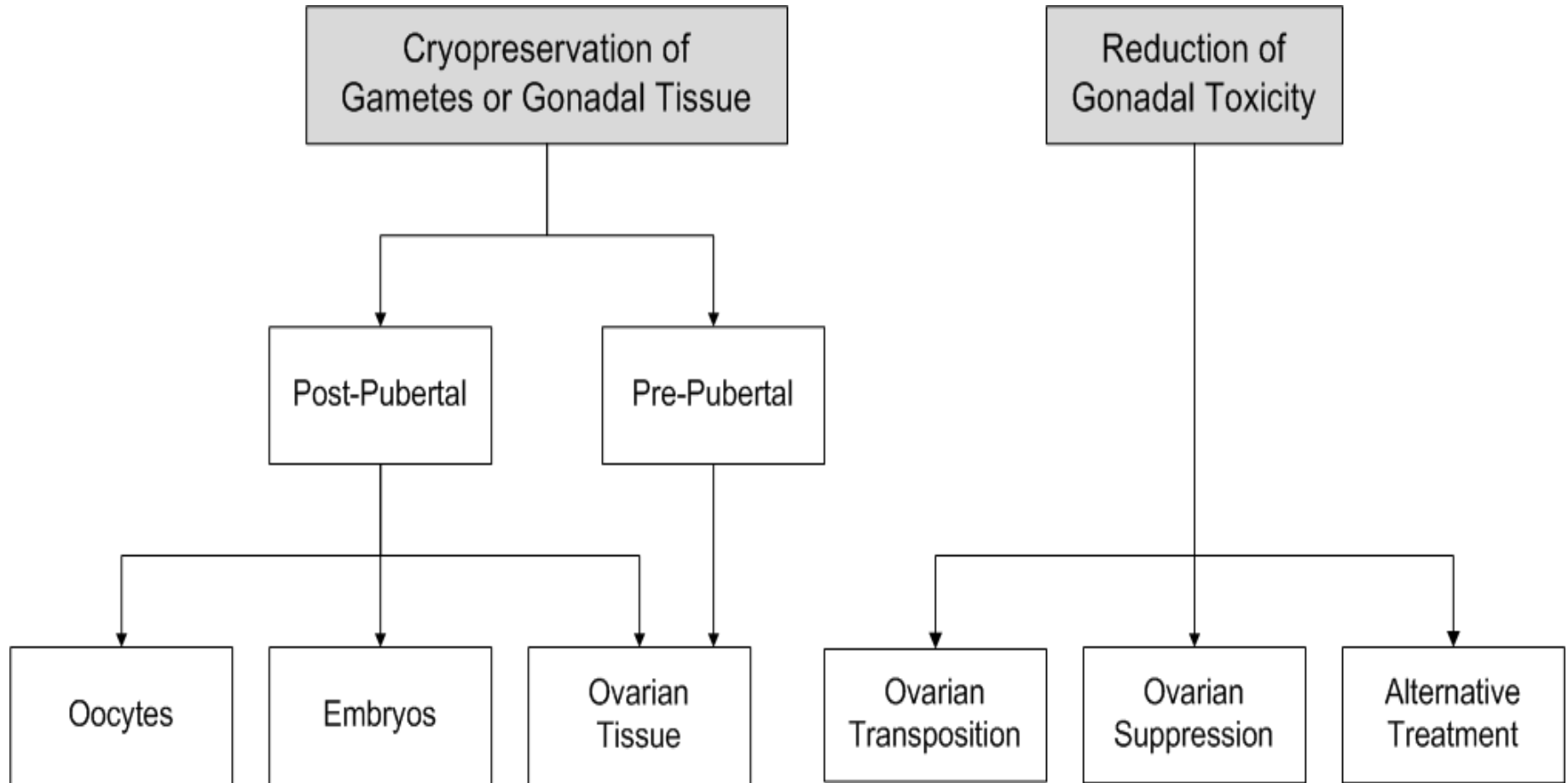
It is impossible to predict with certainty who will be affected permanently

- ▶ Transvaginal ultrasound
 - Ovarian antral follicle count
- ▶ Hormonal analysis
 - Anti-Mullerian Hormone (AMH)
 - Follicle Stimulating Hormone (FSH)
 - Estradiol

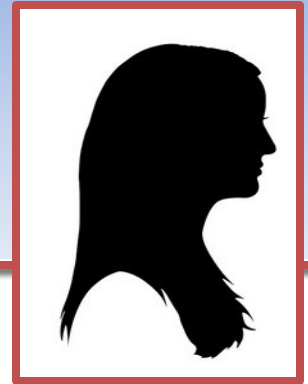


Females

Fertility Preservation Options



Susan



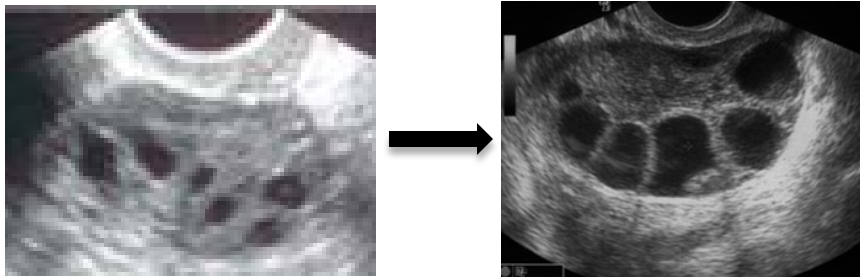
33 year old female

- ▶ Diagnosis: Breast cancer
- ▶ Treatment plan: Mastectomy with immediate reconstruction followed by AC-T (doxorubicin, cyclophosphamide, paclitaxel) → tamoxifen
- ▶ Social: married, 1 child

What is available for this patient?

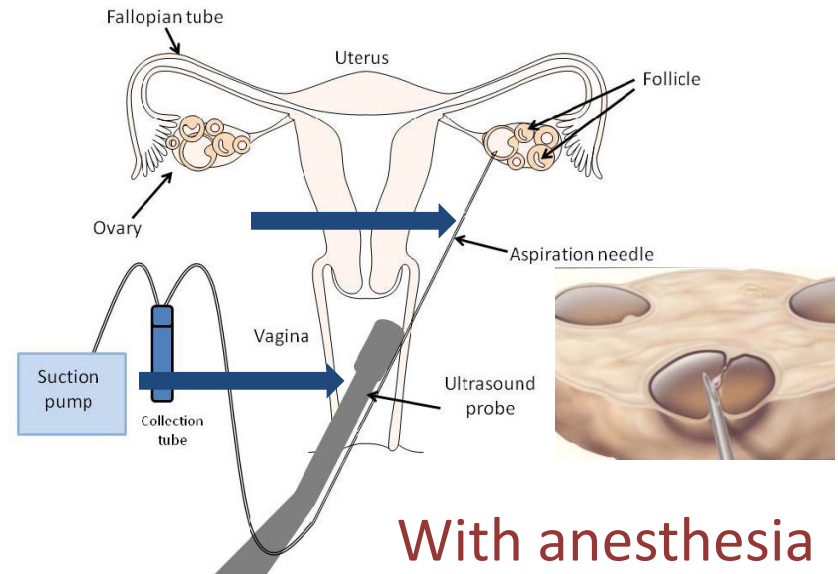
Embryo Cryopreservation

Ovarian
Stimulation



Daily hormone injections
Starts day 2 of menses
Continues for ~10 days

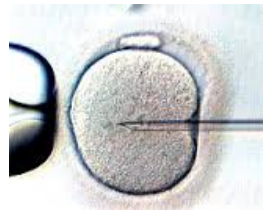
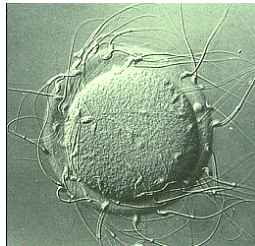
Oocyte
Retrieval



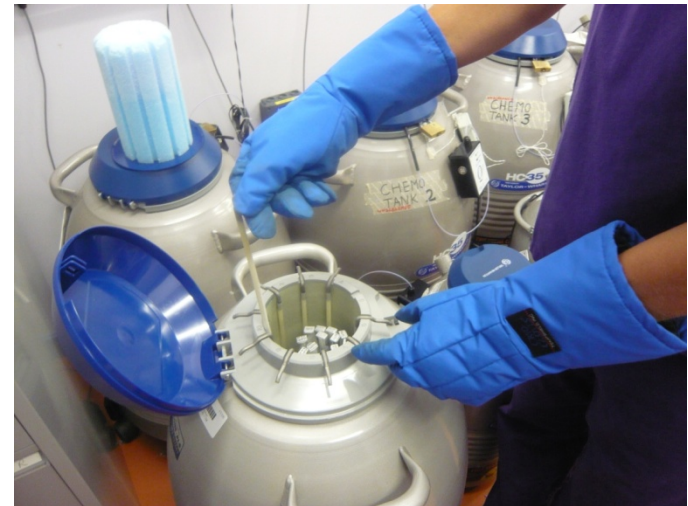
With anesthesia

Embryo Cryopreservation

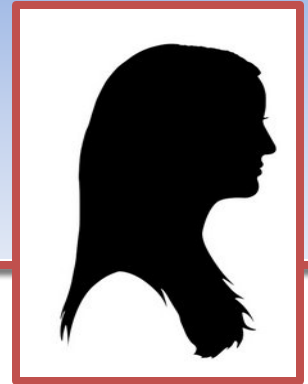
**In Vitro
Fertilization**



**Cryo-
preservation**



Kelly



18 year old female

- ▶ Diagnosis: Relapsed Hodgkin Lymphoma
- ▶ Prior treatment: ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) 2 years ago
- ▶ Treatment plan: BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)
- ▶ Social: single college student, no children

What is available for this patient?

Oocyte Cryopreservation

~~In Vitro
Fertilization~~ →

Cryo-
preservation



Embryo/Oocyte Cryopreservation

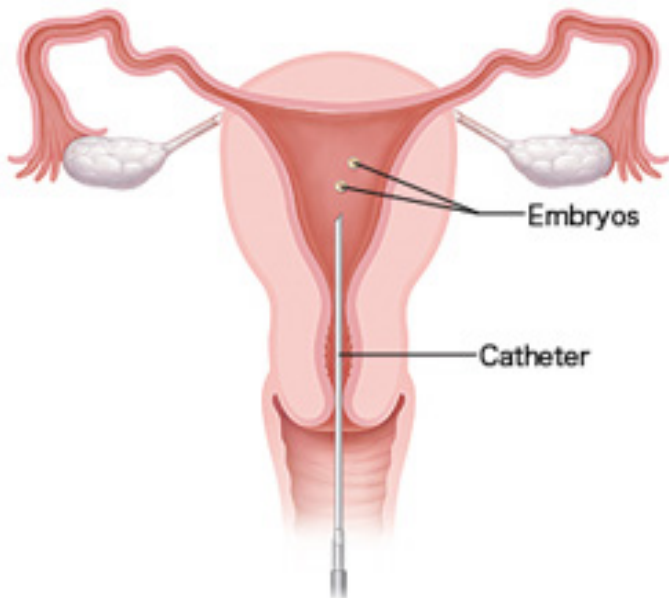
- ▶ Concerns about delay in treatment
 - Generally requires about 3 weeks of time
 - Expedited referrals
 - Downregulation of pituitary with GnRHa
- ▶ Concerns about ↑ estrogen
 - No evidence about effect on recurrence/survival
 - Aromatase inhibitor (eg, letrozole) can lower estrogen levels

Embryo/Oocyte Cryopreservation

- ▶ Concerns about specific medical risks
 - Bleeding if thrombocytopenic or liver dysfunction
 - Infection if neutropenic
 - History of DVT/VTE
 - Anesthesia complications because of disease in the chest

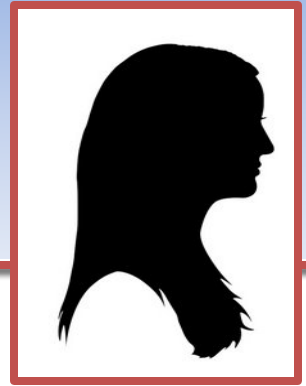
Embryo Transfer

Success Rates with Thawed Embryos
From Non-Donor Oocytes
% Transfers Resulting in Live Births



<35	35-37	38-40	41-42
39.3%	35.7%	30.3%	24.5%

Stephanie



18 year old female

- ▶ Diagnosis: Non-Hodgkin Lymphoma
- ▶ Treatment plan: BEAM (BCNU, etoposide, cytarabine, melphalan), must start within 5 days
- ▶ Social: single college student, no children

What is available for this patient?

Ovarian Tissue Cryopreservation

- ▶ Ovary resected, cortex dissected, frozen, and stored for potential future use
 - Tissue reimplantation – ~20 live births to date
 - Concern about re-implanting cancer cells
 - In vitro maturation – no live births to date
- ▶ Investigational

Ovarian Suppression

GnRH agonist (leuprolide)

- To prevent recruitment of follicles, potentially protecting them from effects of chemotherapy
- Initiated 2-4 weeks before starting chemotherapy, continued monthly throughout treatment
- Investigational - studied primarily in breast cancer and lymphoma with conflicting results

Barbara



3 year old female

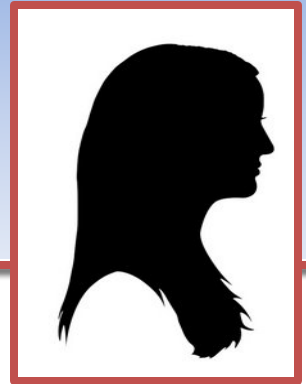
- ▶ Diagnosis: Neuroblastoma
- ▶ Treatment plan: RT and multiagent chemotherapy
- ▶ Social: pre-school child

What is available for this patient?

Ovarian Tissue Cryopreservation

- ▶ Ovary resected, cortex dissected, frozen, and stored for potential future use
 - Tissue reimplantation – no live births to date
 - Concern about re-implanting cancer cells
 - In vitro maturation – no live births to date
- ▶ Investigational

Ellen



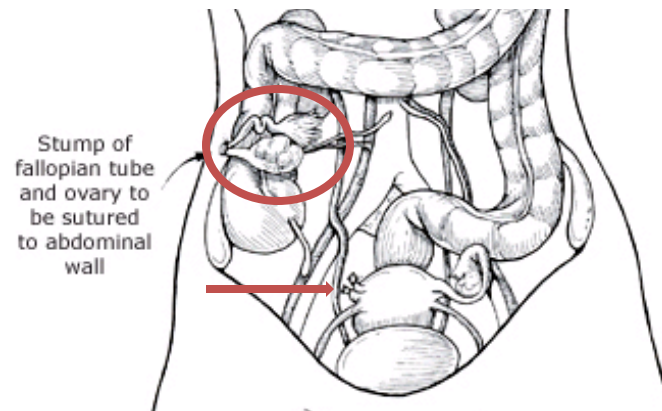
28 year old female

- ▶ Diagnosis: Leiomyosarcoma of bladder
- ▶ Treatment plan: Pelvic RT with gemcitabine, followed by partial cystectomy
- ▶ Social: married, 2 year old daughter

What is available for this patient?

Ovarian Transposition

Prior to pelvic/inguinal field radiation



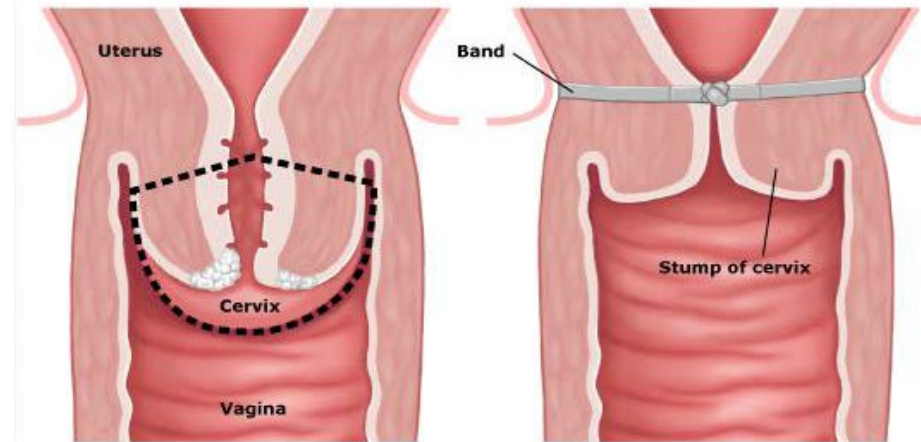
- With IMRT to minimize ovarian & uterine dose
- Also consider embryo/oocyte cryopreservation
- If IVF needed in the future patient will need transabdominal retrieval
- Does not protect the uterus

Alternative Treatment For Select Patients

- ▶ Early stage cervical cancer
Radical Trachelectomy

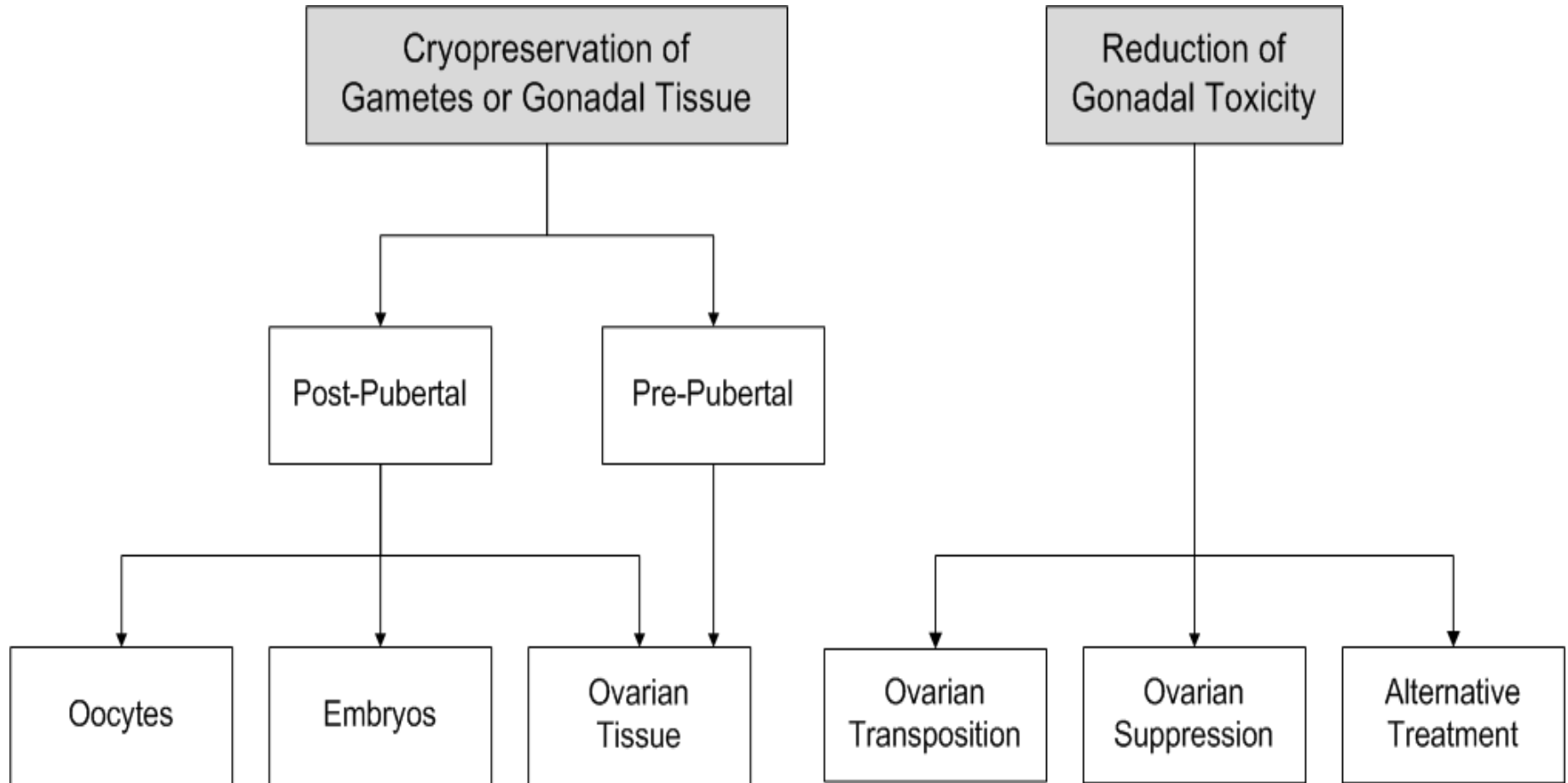
- ▶ Rectal cancer
No pelvic radiation

- ▶ Non-gonadotoxic chemotherapy regimen



Females

Fertility Preservation Options



What does this mean for you?

Recognize that despite your personal assumptions about which patients may be interested in fertility preservation, the following factors may NOT be significant from the patient's perspective:

- Age
- Previous children
- Religious and ethical beliefs
- Advanced disease
- Limited financial resources

What does this mean for you?

- ▶ Initiate the discussion in those at risk
 - Inform patient of risk of infertility
 - Assess interest in future parenting
 - Explain options for fertility preservation
- ▶ Refer patients interested in learning more or who want to pursue fertility preservation

The goal is to ensure patients have the opportunity to participate in the decision-making – to avoid regret in the future