

Breast Cancer, Fertility and Pregnancy

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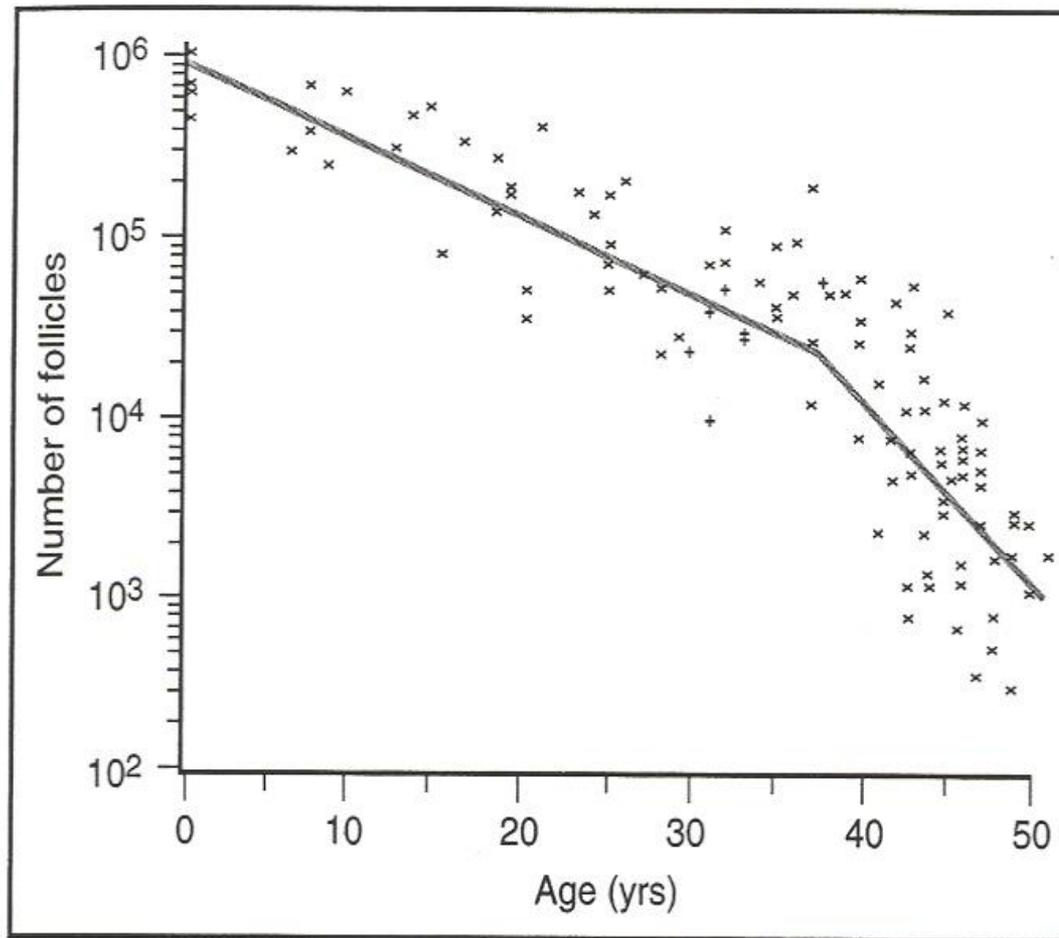
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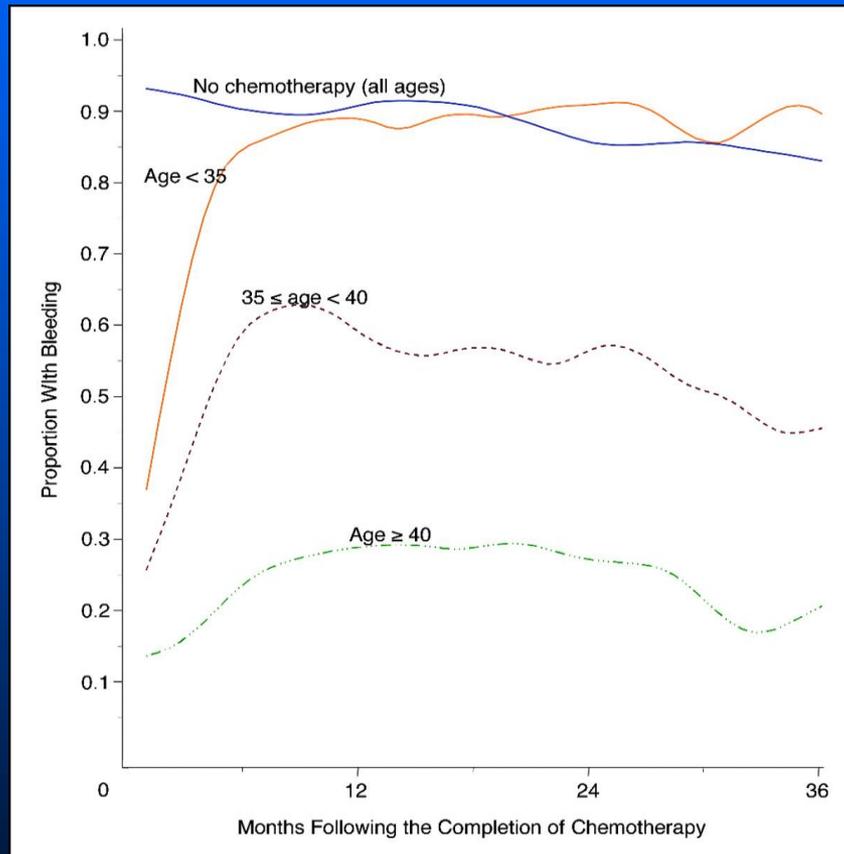
Number of follicles in the human ovary as a function of chronological age. The figure depicts the "broken-stick" regression. (Reprinted from Faddy MJ. Follicle dynamics during ovarian aging. *Mol Cell Endocrinol* 163:43-48, 2000, with permission.)

(From Strauss JF III, Williams CJ. *The ovarian life cycle. Yen and Jaffe's Reproductive Endocrinology; Physiology, Pathophysiology, and Clinical Management.* JF Strauss, RL Barbieri (eds.). Elsevier Sanders, Philadelphia, 2004; pp. 213-254).

Chemotherapy and Ovarian Failure

- Alkylating agents have the best documented and most profound effects on loss of eggs in the ovaries
- Effects depends on patient age and dose
- Loss of eggs rapid in late 30s and early 40s, so effect more significant at these ages when there are already fewer eggs present

Menstrual Bleeding by Patient Age



Menstrual Periods \neq Fertility

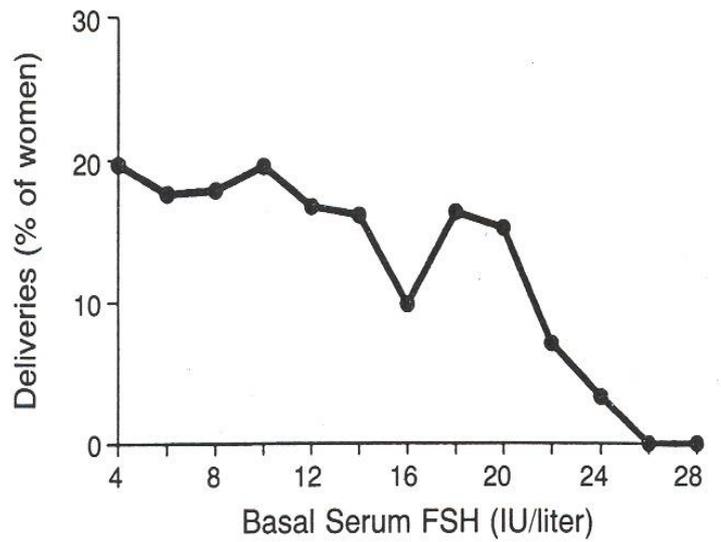
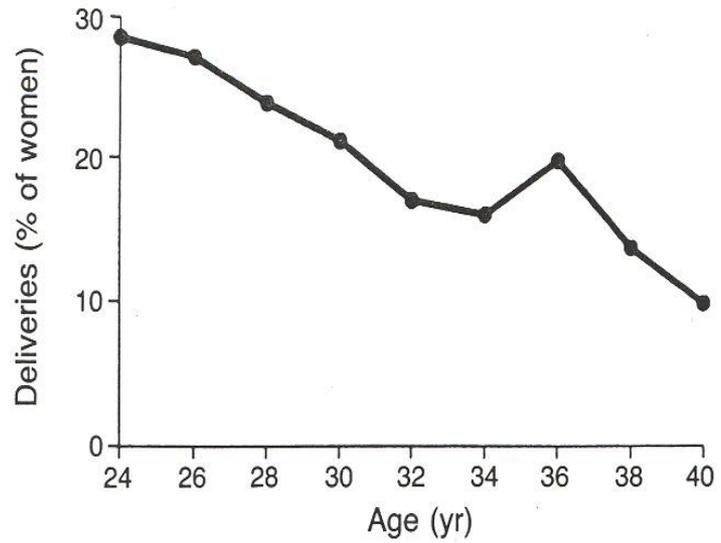
- With the presence of menopausal sx CRA generally represents menopausal status
- Menstrual periods are not particularly good predictors of fertility
- Duration of time between end of treatment and pregnancy increases risk of infertility, eg TAM

Ovarian Reserve Testing

- Anti Mullerian Hormone (AMH)
 - Secreted by granulosa cells that line the follicles
 - Test any time in cycle;
 - some variability in women with normal ovarian reserve
 - minimal variability in women with low levels
 - no clear cutoff; **<0.9 ng/mL low**
- CD 3 antral follicle count (>5 follicles 3-10 mm)

Ovarian Reserve Testing

- FSH: produced by pituitary
 - Stimulates oocyte recruitment and maturation
 - Varies greatly throughout menstrual cycle with midcycle peak
 - Fewer oocytes in ovaries leads to higher FSH
 - CD3 FSH normal: **<10 mIU/ mL** and estradiol **<50 pg/mL** (can be done day 2-4)
- NOT good predictors of spontaneous pregnancy
- Very good predictors of responses to fertility medications

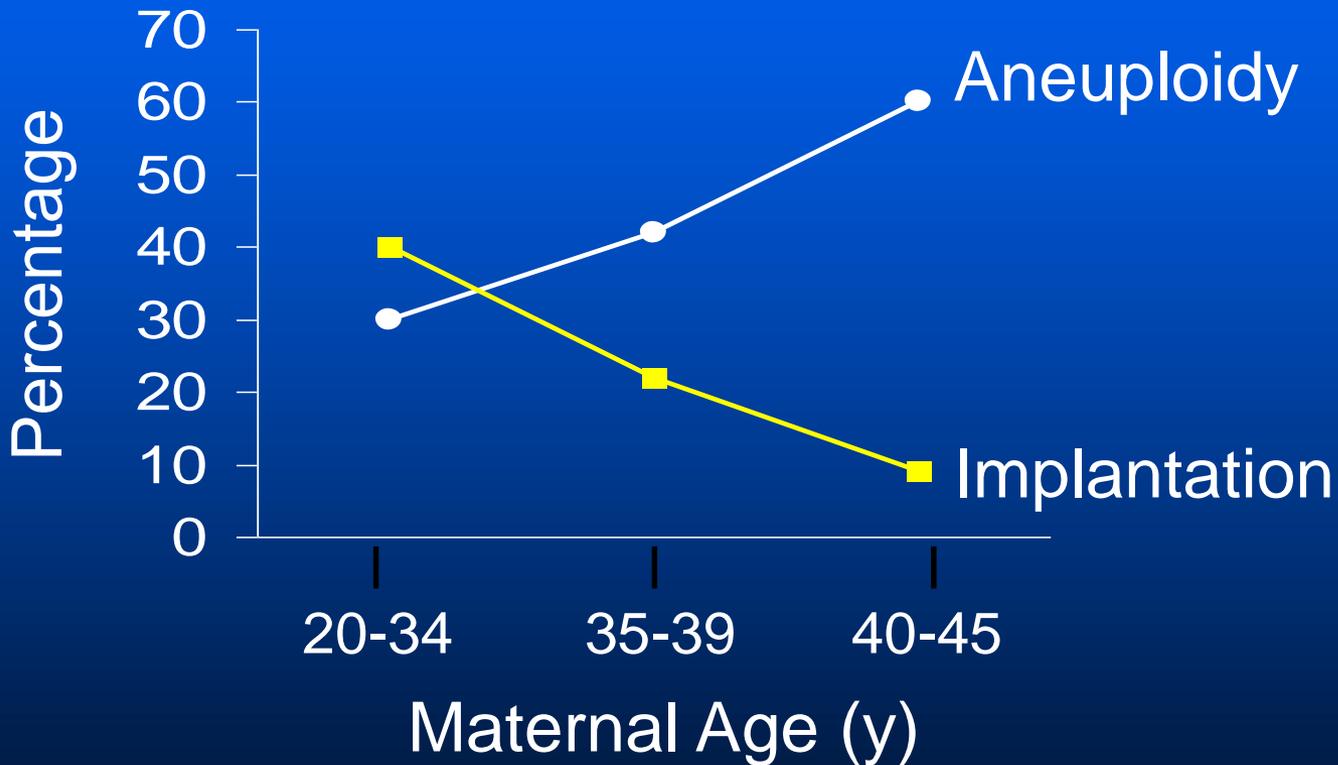


Changes in Rates of Successful Pregnancy According to the Age of the Patient and the Basal Serum Concentration of Follicle-Stimulating Hormone (FSH) during In Vitro Fertilization Cycles.

FSH is an indicator of ovarian age.¹²

Aneuploidy in Human Oocytes

Impact on Implantation Rates from IVF



Munne et al '01,'04,'06

Pregnancy Rates After Breast Cancer

- Available data suggest a ~ 5-15% pregnancy rate after breast cancer
- A survey study showed that 57% of 60 young women trying to conceive after treatment were successful

Fox et al., ASCO 2003; Partridge et al., ASCO 2004; Petrek, Personal Communication March 2005; Ives et al., BMJ 2007; Dalberg PLoSMed 2006; *Partridge et al 2008

What You Should Know

- The rate of infertility in the general population is 15%
 - ie 85% of women are able to conceive on their own
- Ovulation typically occurs 14 days PRIOR to day 1 of the next period.
 - For women with irregular cycles it is difficult to time intercourse

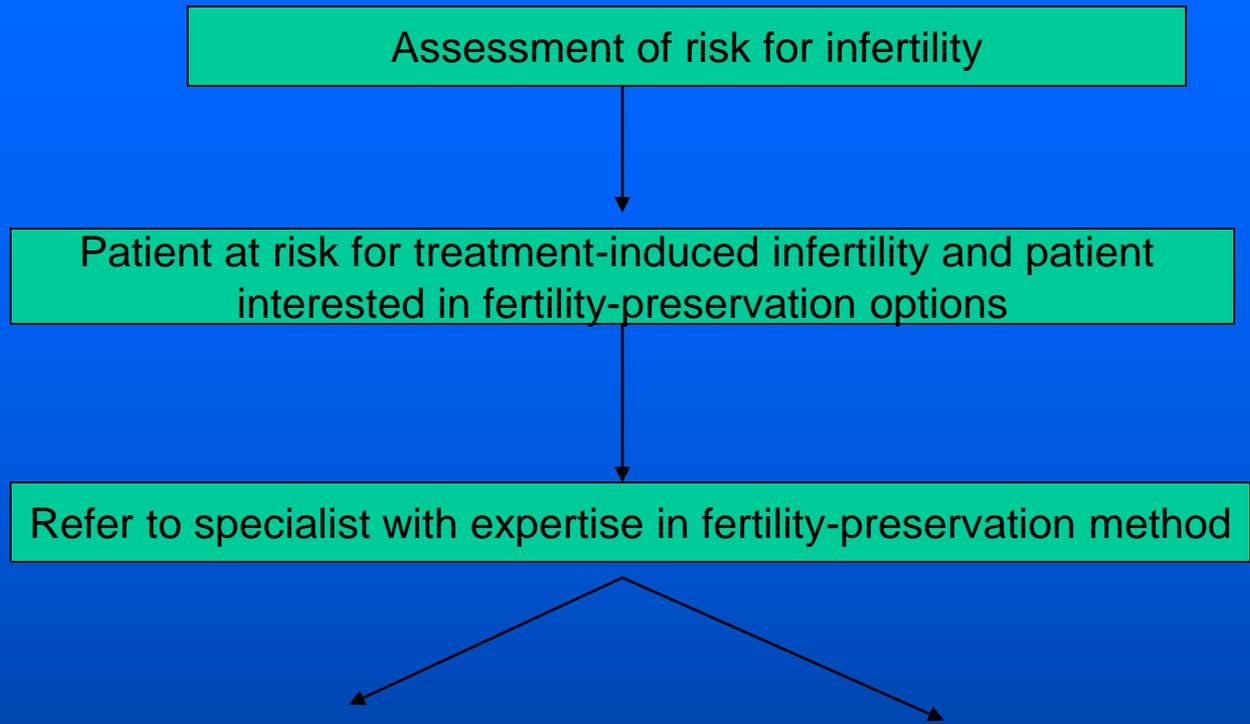
Contributors to Infertility In Cancer Survivors

- Need to delay conception until after time of most recurrences (≥ 2 years)
 - **Advanced maternal age**
- Use of Tamoxifen x 5 years post chemo in premenopausal breast cancer
- MD and patient concern about effects of pregnancy on cancer recurrence
- Patients' concerns that chemo may have mutated remaining sperm or oocytes, or that children may get cancer

Pregnancy After Breast Cancer

- There is no evidence that pregnancy increases the risk of breast cancer recurrence
 - However women who do become pregnant may be in some way different than women who do not
 - Oncologists may be good at determining who may safely become pregnant and who not
- It is more difficult to diagnose breast cancer in women who are pregnant
 - Breasts are full and lumpy
 - Mammography not as accurate

Increasing Likelihood of Future Pregnancy



Eligible for proven fertility preservation method

- Male
 - Sperm Cryopreservation
- Female
 - Embryo Cryopreservation
 - Conservative gynecologic surgery
 - Oophoropexy (RT only)

Investigative fertility preservation techniques

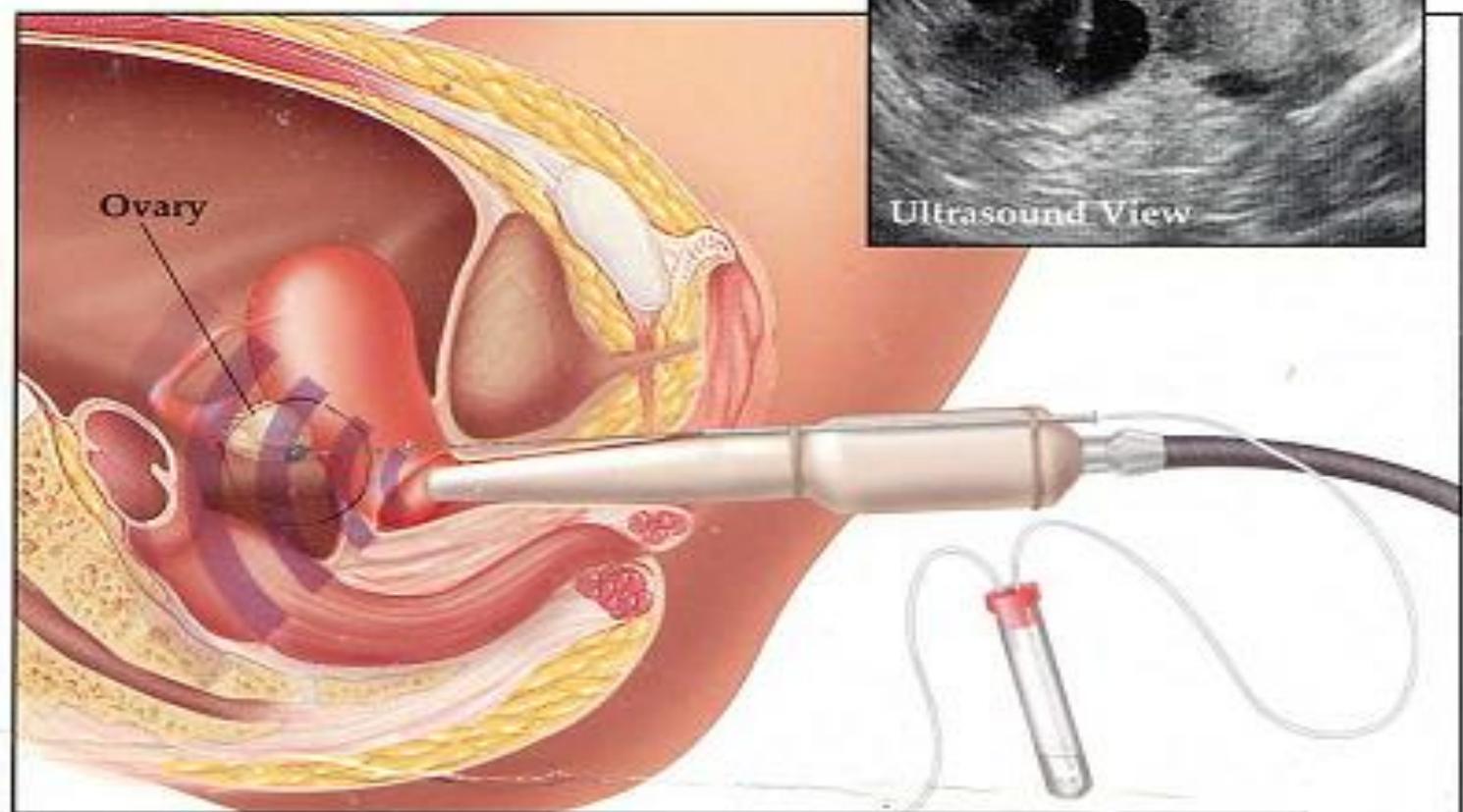
- Female
 - Cryopreservation of oocytes
 - Ovarian Suppression
 - Cryopreservation of ovarian tissue

IVF Before Chemotherapy

- Male partner or willingness to use donor sperm
- 14 days to stimulate ovaries and retrieve eggs using injected FSH \pm LH medications (gonadotropins)
- Often use letrozole to keep estrogen levels low if ER positive breast cancer
- Frequent transvag ultrasounds and blood testing
 - Effect on breast cancer unknown

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- Frequent transvaginal ultrasounds and blood testing
- Eggs removed from ovaries by day surgery procedure
- Eggs fertilized with sperm and then frozen
 - Effect on breast cancer unknown
- About 50% of women who freeze embryos have a baby from them



Using ultrasound to view the ovary, the physician inserts the needle through the wall of the vagina into the ovary and removes the egg for use in IVF or GIFT.

Egg Freezing Before Chemotherapy

- Same as IVF but eggs are frozen without being fertilized
- In future eggs are thawed and fertilized
- Embryos are replaced in the uterus with an outpatient procedure, no anesthesia needed

If Menopause Occurs: Donor Egg

- Pregnancy rate related to age of the donor; age of the recipient does not matter
- Approx 50% cycle, or 80% per stimulation
- Age cut-off at BWH is 49 for intended parent

Resources

- Eginsburg@partners.org
- **617-732-5700 pager 13075**
- **bhammond@partners.org**
- www.resolve.org
- www.fertilehope.org