FERTILITY PRESERVATION:

1. Prevention
2. Protection
3. Preservation
A U.S. Supreme Court opinion agreed with a lower court statement that reproduction is a major life activity and confirmed that conditions that interfere with reproduction should be regarded as disabilities, as defined in the Americans with Disabilities Act.

FERTILITY PRESERVATION:

1. Prevention
CDC ACTION PLAN

- Promoting healthy behaviors that can help maintain and preserve fertility.
- Promoting prevention, early detection, and treatment of medical conditions that can threaten fertility.
- Reducing exposures to environmental, occupational, infectious, and iatrogenic agents that can threaten fertility.
HAZARDS THAT CAN REDUCE FERTILITY IN WOMEN

cancer treatment drugs, including antineoplastic drugs
lead
ionizing radiation, including x-rays and gamma rays
nitrous oxide (N2O)
Hazards that can disrupt the menstrual cycle and/or sex hormone production
a variety of pesticides
carbon disulfide (CS2)
polychlorinated biphenyls (PCBs)
organic solvents
jet fuel
shift work

PREVENTING TUBAL INFERTILITY

• 18% of infertility is due to tubal disease
• Over 1 million new cases of chlamydia reported to CDC each year
• 12% of the patients had infertility following
• Risk of ectopic pregnancy also increases
• Screening by urine PCR is easy and very sensitive
• Treatment: azithromycin 1 gram in a single dose or doxycycline 100 BID for 7 days or
• erythromycin base 500 mg QID, erythromycin ethylsuccinate 800 gm QID or ofloxacin 300 mg BID.
IMPACT OF SMOKING ON FERTILITY

- Menopause occurs 1 to 4 years sooner in smokers than non-smokers
- Infertility rates in men and women are twice the rate of non-smokers
- Smoking accelerates ovarian follicle depletion
- Mutagenic potential of tobacco smoke on gametes
- Increase in miscarriage and aneuploidy rates
- Placental insufficiency and IUGR
- Increase in SIDS and childhood asthma

IMPACT OF WEIGHT ON FERTILITY

12% of infertility is related to a woman weighing too much or too little
- PCOS is the most common cause of anovulation in women of reproductive age
- Obesity increases risk during pregnancy for miscarriage, GDM, macrosomia, caesarian section, and unexplained fetal death
- Increased circulating insulin and chronically elevated estrogen levels through peripheral aromatization leads to increased ovarian androgen production
- A 5-10% weight loss results in improved ovulation and pregnancy rates

Pei-Li Huang, MD  Massachusetts Medical Society
IMPACT OF AGE ON FERTILITY

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AGE AND FECUNDITY

Women >35 should receive evaluation after 6 months of infertility
Women >40 should receive immediate consultation

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FERTILITY SPARING SURGERY

- BORDERLINE OVARIAN TUMORS
  LAPAROSCOPIC STAGING, OVARIAN CYSTECTOMY OR USB

CERVICAL CANCER:
EXCISIONAL CONE, RADICAL TRACHECTOMY

ADENOCARCINOMA OF ENDOMETRIUM AND ATYPICAL HYPERPLASIA
HIGH DOSE PROGESTIN, PROGESTERONE IUD

FIBROIDS
MYOMECTOMY

ENDOMETRIOSIS
LAPAROSCOPY, GnRH AGONIST

FERTILITY PRESERVATION:

2. Protection
OVARIAN FAILURE: WHO IS AT RISK?

Breast cancer
Endometrial cancer
Pelvic irradiation
Benign radical surgery
Lymphoma patients
Leukemia patients
Stem Cell Replacement
BRAC1 patients undergoing prophylactic surgery
Autoimmune and Hematologic Disorders

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GNRH AGONISTS FOR PREVENTION OF POF

Del Maestro et al JAMA July 2011:
A parallel, randomized, open-label superiority trial of Triptorelin for premenopausal women with breast cancer, planning chemotherapy.

281 women were randomized, and 12 months after their last dose of chemotherapy, the rate of early menopause was 25.9% in the women with chemotherapy alone, versus 9.8% in the chemotherapy plus Triptorelin group, for an absolute difference of -17%.

A systemic review and meta-analysis of 13 studies (3 randomized controlled trials and 10 non-randomized studies) showed that GnRH agonist treatment resulted in a higher likelihood of preserved ovarian function. However, when limited to only randomized-controlled trials, there was no statistically significant difference.

Currently ASRM and ASCO do NOT recommend GnRH agonists for fertility treatment during chemotherapy.

Pei-Li Huang, MD
Massachusetts Medical Society
FERTILITY PRESERVATION:

3. CRYOPRESERVATION

Pei-Li Huang, MD

Bedoschi and Oktay, Fertility and Sterility, May 2013
OVARIAN TISSUE TRANSPLANTATION

Cryopreservation of ovarian tissue: 3 options

- Cortical ovarian biopsy
  - Fragments
  - Isolation
  - Avascular transplantation
    - Orthotopic
    - Heterotopic
  - 13 Livebirths
  - AVOIDS TRANSMISSION OF MALIGNANT CELLS

- Isolated follicles
  - In vitro culture
  - Avascular transplantation

- Whole ovary
  - Vascular transplantation
  - AVOIDS FOLLICULAR LOSS DUE TO ISCHEMIA

IVF PROTOCOLS FOR CANCER PATIENTS

- OVARIAN STIMULATION CAN START AT ANY TIME POINT IN THE CYCLE
- USE OF LETROZOLE AND LOW DOSE GONADOTROPINS REDUCE ESTROGEN EXPOSURE
- MULTIPLE BACK TO BACK CYCLES CAN BE COMPLETED PRIOR TO CHEMOTHERAPY
WHO IS A CANDIDATE FOR EGG FREEZING?

- Patients receiving gonadotoxic therapies: cancer and medical conditions
- Patients with genetic conditions: eg. BRAC mutations
- Failure to obtain sperm for IVF
- Cryopreservation of eggs for those unable/unwilling to freeze embryos
- Women willing to donate eggs
- Elective cryopreservation to defer childbearing

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FACEBOOK AND APPLE HAVE ANNOUNCED THEY WILL COVER UP TO $20,000 FOR EGG FREEZING
IDENTIFYING OOCYTES FROM FOLLICULAR FLUID

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A MATURE OOCYTE

Pei-Li Huang, MD

VITRIFICATION VS SLOW FREEZE TECHNIQUES

VITRIFICATION
- Higher cryoprotectant concentration
- Lower cryodamage
- 95% oocytes survive thaw
- More clinical expertise
- More time
- Less equipment
- Closed or open system

SLOW FREEZE
- Lower cryoprotectant concentration
- Higher cryodamage
- 45-46% oocytes survive thaw
- Easier to perform
- Less time
- Freezing machine required
- Closed system

VITRIFICATION VS SLOW FREEZE TECHNIQUES

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THAWED TISSUE: SLOW FREEZE VS VITRIFICATION

CULTURING EMBRYOS IN MICROINCUBATORS
LOADING EGGS INTO A CYROTOP

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FILLING THE TABLE TOP DEWAR WITH LIQUID NITROGEN

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EGGS ARE FLASH FROZEN IN LIQUID NITROGEN

INSERTING THE CRYOTOP INTO A SLEEVE
THE GOBLET AND CANE

LOADING THE CANE INTO THE CRYOTANK
OOYCTE FREEZING : SUCCESS RATES

• 1996 FIRST BABY REPORTED FROM A FROZEN OOYCTE
• 92-95% SURVIVAL RATE OF VITRIFIED WARMED OO CYTES
• NO DIFFERENCE IN FERTILIZATION AND PREGNANCY RATES WHEN ICSI USED WITH WARMED OO CYTES AS COMPARED TO FRESH
• SUCCESS RATES DECLINE WITH MATERNAL AGE
• NO DIFFERENCE IN CONGENITAL ANOMALIES OR BIRTH WEIGHT
• LIMITED SHORT TERM FOLLOW UP
• SURVIVAL, FERTILIZATION, IMPLANTATION AND PREGNANCY RATES IN OO CYTES THAWED UP TO 48 MONTHS LATER ARE THE SAME AS COMPARED TO THOSE FROM EARLIER THAWS

THE FUTURE OF REPRODUCTIVE MEDICINE

▶ ROBOT ASSISTED LABORATORY TECHNIQUES AND MONITORING
▶ IMPROVING THE IMPLANTATION RATE – AN END TO MULTIPLE BIRTHS?
▶ OVARIAN GERM LINE STEM CELLS– AN UNLIMITED SUPPLY OF OO CYTES?