Infertility and the Role of the Primary Care Provider

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Objectives

- Definitions of Infertility
- Frequency of Infertility
- Causes of Infertility
- Infertility Evaluation
  - Questions to ask
  - Physical examination
  - Pre-pregnancy Counseling
  - Additional testing
- What to do with an infertile patient
- Age-related fertility decline
- Limitations for offering oocyte cryopreservation
- What does the process entail?
- Where does the general practitioner fit in?
- What fertility screening should I do?
- Summary

Definitions

- Infertility: failure to achieve pregnancy within 12 months of unprotected intercourse or therapeutic donor insemination in women younger than 35 years
  - Or within 6 months in women older than 35 years
- In women older than 40 years, evaluation and treatment is warranted immediately
  - Also is immediately warranted in women with a condition known to cause infertility

Frequency of Primary Infertility

- Different per country
- In married women in USA:
  - 7.3-9.1% in women ages 15-34
  - 25% in women 35-39 years old
  - 30% in women 40-44 years old

Causes of Infertility

- Male Factor
- Ovarian Dysfunction
- Tubal Damage
- Endometriosis
- Cervical Problems
- Unexplained
### Comprehensive medical history
- BOTH male and female partners
  1. Duration of infertility
  2. Results of any prior evaluation or treatment
  3. Menstrual history
    1. Menarche
    2. Cycle length
    3. Bleeding patterns, presence of dysmenorrhea
    4. Signs of ovulation
  4. Pregnancy history
    1. Gravity, parity
    2. Time to pregnancy; need for assistance
    3. Same or different partner
    4. Route of delivery
    5. Complications
  5. Coital timing and frequency
  6. Past Medical History
    1. Medical illness
    2. Surgeries
    3. Injuries
  7. Gynecologic history
    - STIs, PID, endometriosis, fibroids
  8. Medications and allergies
  9. Family history
    - Early menopause, birth defects, developmental delay, reproductive issues
  10. Known hazards
      - Occupational, environmental
  11. Social history
      - Nicotine, alcohol, other recreational or illicit substances

### Evaluation

#### Specific to male partner
1. Erectile or ejaculation issues
2. Prior fertility
3. Use of anabolic steroids or testosterone
4. Exposure to gonadal toxins or trauma

### Physical Examination

- Weight/Body Mass Index, blood pressure, pulse
- Thyroid – enlargement, nodularity, tenderness
- Breast – presence of secretions
- Signs of androgen excess
- Vaginal or cervical abnormalities, secretions, or discharge
- Pelvic or abdominal tenderness, organ enlargement, or masses
- Uterus – size, shape, mobility

### Pre-pregnancy Evaluation

- Optimize health, including pre-existing medical conditions
- Discuss infectious disease screening
- Update immunizations
- Discuss genetic carrier screening
- Discuss prenatal vitamins/folic acid
- Review modifiable risk factors
- Screen for intimate partner violence

### Testing Considerations

- Driven in part by findings in history and exam
- Thyroid stimulating hormone
- Ultrasound
- Hysterosalpingogram
- Ovarian reserve testing
- For male: semen analysis
# Testing Considerations

**Box 1. Infertility Tests That Should Not Be Routinely Ordered**
- Laparoscopy for unexplained infertility
- Advanced sperm function testing (e.g., DNA fragmentation testing)
- Proctosigmoid testing
- Thrombophilia testing
- Immunologic testing
- Karyotyping
- Endometrial biopsy
- Proctitis


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# Treatment

- Treatment largely depends on the cause of infertility
- For a young couple who has not yet tried to conceive for at least 12 months, consider educating about timed intercourse and use of urinary ovulation prediction kits
- If abnormalities on testing, refer!
- Delayed evaluation and treatment of an infertile woman in her mid-thirties or older may lower the patient’s chances of success once therapy is initiated
- Referral to reproductive endocrinology and infertility is never a bad idea! If no specialist close by, can consider referral to general OB/GYN

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# Update on Infertility: age-related fertility decline and planned oocyte cryopreservation

- Birth rates for teens and 20-somethings at record lows
- Birth rates for those in their 30s and 40s are at their highest since the 1960s
- Average age of 1st time mother in USA: 26.6 (record high)
- What is causing this trend?

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# Planned Oocyte Cryopreservation - Rationale

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# Planned Oocyte Cryopreservation - Rationale

- Improvements in contraception
- Improvements in access to contraception
- Decision to delay childbearing until certain goals are met
  - Educational
  - Financial
  - Career
- Most women state that they are waiting for the right partner before pursuing pregnancy

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# Rationale for oocyte cryopreservation

**“Need-based”**

**Versus**

**Planned oocyte cryopreservation, also known as “social egg freezing”, “elective”, “prevention of anticipated gamete exhaustion”**

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Planned Oocyte Cryopreservation - Rationale

Women may also have unrealistic expectations of female reproductive potential with age

AND

The ability of reproductive medicine to restore that potential

Preventive medicine?

As women often delay childbirth for reasons outside of their control, there has been a push to move away from terminology suggesting that planned oocyte cryopreservation is “elective”, “social”, or “non-medical”, but rather as possible preventive medicine for anticipated gamete exhaustion

Age limitations?

• The suitable range of ages are still being determined – no recommendations as of yet

• The American Society for Reproductive Medicine (ASRM) prefers that those who wish to be oocyte donors donate between the ages of 21 and 34, to decrease the cytogenetic risks associated with oocyte age

Cost-effectiveness?

• Least cost-effective for ages 25-30

• If a patient requires marriage before attempting pregnancy, oocyte cryopreservation is most cost-effective at age 35

• model accounted for probability of marriage

• If a patient does not require marriage before attempting pregnancy, oocyte cryopreservation is most cost-effective at age 37

Age limitations?

• Keep in mind: the older the patient, the more oocytes she will need to store for a reasonable chance of a live birth

• Also, the older the patient, the more likely she will need several cycles to achieve enough oocytes to have a reasonable chance of a live birth

• At age 38, a patient may need to store ~25-30 oocytes for a reasonable chance of a live birth
Other Limitations

- Expensive and often self-pay
- May need several cycles for a reasonable chance of a live birth
- May be unnecessary if patient never uses the oocytes
- Possible feelings of regret
  - Often due to having fewer oocytes for freezing and inadequate information or emotional support

Oocyte Cryopreservation in the Media

- KUWTK

What does the process entail?

Initial consultation

Start pre-medications
  - Sometimes OCPs
  - Sometimes lupron
  - Sometimes nothing!

Start stimulation medications
  - Usually 8-12 days
  - Monitoring
  - Labs
  - Ultrasound

Trigger shot!

Oocyte retrieval and cryopreservation

Figure 48: Numbers of ART Cycles Performed for Banking All Fresh Non donor Eggs or Embryos, 2007-2016

CDC Data, 2007-2016

The Modern Family star told Good Morning America in 2013 that she froze her eggs in hopes of having a baby with her then-fiancé, Nicholas Loeb. According to People, Sofia has a 24-year-old son from her first marriage, which ended in 1993.

“I wanted to make sure I already froze my eggs. I wanted to take advantage of science,” she said. “I took them out already. They're in the refrigerators. Hopefully, they'll be fresh by the time I use them.” Sofia, then 40, said she wanted to plan ahead because of her age. “Nothing happens that naturally anymore,” she said. (The eggs are currently part of a drawn-out legal battle between Nicholas and Sofia, according to Today—Nicholas wants sole custody of the fertilized eggs they created together.)
**Risks**
- Bleeding
- Infection
- Pain
- Ovarian Hyperstimulation Syndrome (OHSS)
  - Hemoconcentration
  - Third-space accumulation of fluid
- Ovarian torsion
- Failure

**Where does the general practitioner fit in?**
- You are best poised to educate women!
- Older female age can lead to:
  - Reduced egg number
  - Reduced egg quality
  - Increased chromosomal abnormalities
  - Leading to increased fetal anomalies and pregnancy losses
- As time passes, the greater chance that an illness, life circumstance, or accident can impair fertility or increase abnormalities in offspring

**Where does the general gynecologist fit in?**
- Most successful and low-cost way to have a baby: conception through sexual intercourse or donor insemination at an early age (prior to mid-30s)
- Consider referral to mental health provider
  - Explore expectations, motivations
- Consider referral to Reproductive Endocrinology and Infertility
  - Counseling on success rates, expectations, novelty of the procedure

**What fertility screening should I do?**
- Antimullerian hormone (AMH) and antral follicle count (AFC) are used as predictors of ovarian reserve in infertile populations
- The use of AMH is not recommended as a routine screening tool in low-risk patients
  -Shown to have too high of variability in fertile women to be a good fertility index
  -If your patient has not tried to conceive, you won’t know if she’s fertile or not
  -Don’t want to scare patient or give false reassurance

- AFC does not reliably predict failure to conceive
- A single follicle-stimulating hormone (FSH) has limited reliability
- Inhibin B is also not a reliable measure of ovarian reserve
- Basically, there are no good predictors for pregnancy in those who haven’t tried
- Always a discussion with the patient

**What fertility screening should I do?**
- Prompt workup and referral is recommended for infertile couples
- Young women may consider oocyte cryopreservation
- Egg freezing is no longer experimental, but it is not perfect
- Best chance of pregnancy is with sexual intercourse or a sperm donor before mid-30s
- Difficult to predict who will have fertility issues later on
- Egg freezing may be preventive medicine for future infertility for the appropriate patient
- Counselling is important!

**Summary**
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Questions?

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