Primary care approach to infertility

Joseph B. Stanford, MD, MSPH
Departments of Family and Preventive Medicine, Obstetrics and Gynecology, and Pediatrics
University of Utah School of Medicine
Objectives

• Describe the incidence, prevalence, and resolution of infertility in the general population.
• Outline the main underlying causes of infertility.
• Describe a primary care approach to evaluating and treating infertility.
Infertility

• Relevance
• Descriptive epidemiology
• Causes
• Primary care approach
  – Lifestyle
  – Diagnosis
  – Treatment
  – Referral
10-15% of couples report that they are unable to have the number of children that they would like to have.
Population-based survey of women age 40-55 in UK for lifetime infertility

16% had consulted doctor for problems conceiving
8% had fertility treatment
2.4% never conceived
1.9% conceived but no live birth

Oakley et al. *Hum Reprod* 2008
Fertility problems are also related to

- Pregnancy loss
- Perinatal outcomes
- Other chronic conditions and health risks in women and men
- Psychological and relationship stress
Fertility (fecundity) is a spectrum

- Matter of probability and time
- The time cutoffs used to identify a fertility problem (usually 1 year) are by convention, not based on any biological threshold.
- It takes two (for natural conception)
- Usually not diagnosed until “trying”
Fertility (fecundity) is a spectrum

“The estimated percentage of infertile couples that would be able to conceive after an additional 12 cycles of trying varied from 43-65% depending on age.”

Dunson et al.  
*Obstet Gynecol* 2004
What is “trying”? 

• “Regular” intercourse without contraception  
  – Once a week? Twice a week? More?  
• Tracking your cycle and ovulation?  
• Intercourse targeted to the fertile window?  
• Common for couples to say: we haven’t (always) been using contraception, but we haven’t started trying yet.
Definitions

• **Primary infertility**: No prior pregnancy (or birth)
• **Secondary infertility**: Prior pregnancy (or birth)
Infertility

- Syndrome, not one disease
- Multiple underlying conditions
- One of our studies of 370 couples, in review, found a mean of 5.5 related diagnoses per couple.
- About half of couples have a male component
Clinical infertility

• ½ of couples ever go to a doctor for advice.
• ½ of those who go to a doctor ever get diagnostic procedures or treatment
• Variation in evaluation and treatment
Lifestyle

• Don’t smoke
• Moderate alcohol and caffeine
• Exercise
• Maintain good metabolic health
Clinical vs. population-based sample  \((n=960)\)

<table>
<thead>
<tr>
<th></th>
<th>Clinic</th>
<th>Population</th>
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<tbody>
<tr>
<td>Ever received medical treatment</td>
<td>91%</td>
<td>59%</td>
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<tr>
<td>Ever had IVF</td>
<td>46%</td>
<td>14%</td>
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<tr>
<td>Had a subsequent live birth</td>
<td>55%</td>
<td>52%</td>
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</tbody>
</table>

Female: common underlying conditions

• Polycystic ovarian syndrome
  – Sporadic or chronic anovulation (longer cycles)
  – Facial hair via excess androgens
  – Multiple small cysts on ovaries, ovaries enlarged
  – Insulin resistance
  – “Ovarian metabolic syndrome”
Female: common underlying conditions

- Ovulatory disorders for other reasons than PCOS
  - Obesity
  - Underweight (eating disorder, others)
  - Thyroid
- Endometriosis
- Prior pelvic infections
- Tobacco, other substances
Male underlying conditions

- Congenital
  - Undescended testicles
  - Microdeletions in Y chromosome
- Varicocele (varicose veins of testes)
- Obesity
- Tobacco
- Androgenic steroids!
Sperm concentrations over time (45 men, 9 months)

Wilcox, 2010
Male fecundability and semen parameters

Wilcox, from Bonde et al. 1988
Fertility awareness

• Menstrual Cycle
  – Starts with menstrual bleeding (visible), but more important event is ovulation

• Fertile window = days of cycle when intercourse likely to result in pregnancy
The menstrual cycle: cycle length

(a) Distribution of cycle length
3137 non-conception cycles, 562 women 18- to 40-y-old

Najmabadi et al.  
*Paed Perinat Epidemiol* 2020
On what day of the cycle does ovulation usually occur?
The menstrual cycle: day of ovulation

(c) Distribution of follicular phase length
3209 ovulatory cycles, 577 women 18- to 40-y-old

Najmabadi et al.  
*Paed Perinat Epidemiol* 2020
What is the typical duration of the luteal (postovulatory) phase?
The menstrual cycle: luteal length

(d) Distribution of luteal phase length
3022 non-conception ovulatory cycles, 555 women 18- to 40-y-old

Najmabadi et al.  
*Paed Perinat Epidemiol* 2020
How many days during the menstrual cycle can a woman (couple) get pregnant?
Probability of clinical pregnancy

Day relative to estimated day of ovulation

Ovarian hormones
Type E and G mucus at the cervix
Type E and G mucus: light microscopy
The fertile window can be early, mid, or late in cycle.
How can a woman identify her ovulation and fertile days?
Fertility awareness

Women and couples can learn to determine their fertile window by observing their own biomarkers.
Identifying the fertile window

• Before ovulation: mucus increases, rise in urinary estrogen, LH surge
• After ovulation: mucus decreases, basal body temperature rises, progesterone metabolites in urine
Fertility awareness- systems

• Standard Days (*cycle beads; only cycles 26-32 days*)
• Dynamic Optimal Timing (*CLUE app*)
• Urine LH tests (*limited window*)
• Peak Day Method (*google: Peak Day Utah*)
• Billings Method or Creighton method
• Marquette Method
• BBT (*retrospective; NaturalCycles app*)
• Sympto-thermal (*Kindara app; TCOYF; CCL*)
### Fertility awareness in women trying to conceive

<table>
<thead>
<tr>
<th>Method</th>
<th>No. of pregnancies</th>
<th>No. of cycles</th>
<th>Adjusted&lt;sup&gt;a&lt;/sup&gt;</th>
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<tr>
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<tr>
<td>No fertility indicator</td>
<td>669</td>
<td>5,464</td>
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Stanford et al. *Fertil Steril* 2019
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Stanford et al. *Fertil Steril* 2019
Primary care approach to the infertile couple
• History
• Physical exam
• Initial laboratory
## History

### Woman
- Reproductive History
- Menstrual History
- GYN History, STIs
- Contraception History
- Major or Chronic Illness
- Family History
- Smoking, Alcohol
- Medications, Supplements
- Hirsutism, Acne
- Weight, Eating Patterns
- Coitus- Lubricants, Pain
- Toxic Exposures?

### Man
- Reproductive History
- Mumps
- Major or Chronic Illness
- Urologic History
- Heat to Testicles
- Smoking, Drugs
- Medications, Supplements
- Erectile Function
- Family History
- Weight, Eating Patterns
- Toxic Exposures?
Physical examination

**Woman**
- Virilization
  - Acne, Hirsutism
- Body Mass Index
- Galactorrhea?
- Thyroid
- Pelvic Examination
  - Anatomic issue?
  - Pain?

**Man**
- Urologic Examination
  - Varicocele?
  - Hypospadias?
Initial laboratory

**Woman**
- **Assess ovulation, fertile window, cycle history**
- Hysterosalpingogram or chlamydia antibody
- Consider TSH, Prolactin
- Evaluate for metabolic abnormalities, **PCOS**

**Man**
- **Semen Analysis**
- Evaluate for metabolic abnormalities
Likelihood of receiving IVF: aOR 0.48 (0.10-0.59)
Restoring underlying health will often improve healthy reproduction
Overall Health

Reproductive and Prenatal Health
Treatment

• Man: lifestyle counseling
  – If varicocele = urology referral
  – Treat underlying conditions

• Woman
  – Learn the cycle and the fertile window
  – Treat underlying conditions
    • PCOS
    • Overweight
    • Thyroid
    • Endometriosis (surgical referral)
Optimized cycles

• Ovulation
• At least one act of intercourse on the highly fertile days
  – 1-2 days prior to ovulation
  – Days of best quality mucus
• Luteal (postovulatory) phase at least 11 days
  – Can support with human progesterone (prometrium, NOT provera)
  – Check progesterone and estradiol levels 7 days after ovulation
• No abnormal spotting/bleeding
• Psychosocial stress addressed!
• If no pregnancy in 6 optimized cycles, refer
Restored mom & dad --> healthier babies

**RRM**
- Low birth wt: <5% 
- Prematurity: <5%

**IVF**
- Low birth wt: ~9%
- Prematurity: ~15%

Sart.org 2018 statistics
• Understanding the fertile window is fundamental to women’s health.
• The fertile window is ~9 days (as identified) and can occur early, middle, or late cycle.
• Primary care should perform the first steps of fertility evaluation, and continue to follow the couple, especially for underlying health conditions.
• joseph.stanford@utah.edu
• South Jordan Clinic, Natural Infertility: 801-213-2996
• medicine.utah.edu/dfpm/public-health/research-service/ocrh/