SECONDARY INFERTILITY

Week 100

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Reading Assignment: ACOG Committee Opinion #781, “Infertility Workup for the Women’s Health Specialist”
LEARNING OBJECTIVES

• To review the definition, common causes, and workup for secondary infertility

• To understand the initial management of secondary infertility
Your patient is a 30 yo G2P1011 woman who presents for a GYN visit. She reports difficulty conceiving with her husband. They have been trying to conceive for 2 years. She has one child with her husband; states she had no difficulty conceiving for that pregnancy. She denies any other issues.
What elements of the patient’s history are most relevant?

- **PMH:** Denies
- **PSH:** D&C for EPF
- **OBHx:** G1-EPF @ 6 weeks; G2-FT NSVD, uncomplicated
- **GynHx:** LMP 2 weeks ago; history of regular cycles; reports dysmenorrhea and heavy menstrual bleeding; denies STIs, abnormal paps, fibroids, cysts; used OCPs in the past for contraception but has not used any BC x 2 years
- **FH:** Mother and sister with fibroids
- **SH:** Denies T/E/D; works as an English professor; lives with husband and son; denies IPV
- **Meds:** Multivitamin
- **All:** Seafood
PHYSICAL EXAMINATION

What elements of the patient’s physical exam are most relevant?

**VS:** BP 138/70, P 77, RR 14, Height 165 cm, Weight 78kg, BMI 28.7 kg/m²

**Gen:** NAD

**HEENT:** oropharynx clear, no thyromegaly, no lymphadenopathy

**Breast:** Normal appearance, symmetric; no masses, lesions, skin changes; nontender to palpation; no discharge

**Chest:** CTAB

**CVS:** RRR

**Abd:** Soft, Nt, ND, no rebound/guarding/masses

**GU:** NEFG, normal appearing cervix, vaginal mucosa; anteverted, 7 week size uterus; no CMT; no uterine or adnexal masses or tenderness

**Ext:** WWP

**Skin:** Normal turgor, no hyperpigmentation
REVIEW: INFERTILITY

What is the definition of infertility?

• Failure to achieve pregnancy within 12 months of unprotected intercourse or donor insemination in women under 35
• OR 6 months for women over 35

• Secondary infertility is infertility (as defined above) after a previous pregnancy or previous ability to carry a pregnancy to a live birth (WHO)
Epidemiology

- **15%** of couples
- Prevalence of 2° infertility varies by region and age
  - United States: < 6%
  - **Increases with increasing age:** 2.6% for 20-24yo, 27.1% for 40-44yo.

Mascarenhas, 2012
REVIEW: ETIOLOGIES OF SECONDARY INFERTILITY

• Female factor
  • Ovulatory dysfunction
  • Tubal factor
  • Uterine factor

• Male factor
  • 40-50% of couples

• Female and male factors

• Unexplained

Flashback to: “Infertility Evaluation” AuduBon-Bon
# REVIEW: EVALUATION

## Table 1. Basic Infertility Evaluation

<table>
<thead>
<tr>
<th>Female</th>
<th>Male</th>
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<tbody>
<tr>
<td><strong>History</strong></td>
<td><strong>History</strong></td>
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<td></td>
<td><strong>Semen analysis</strong></td>
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<td><strong>Physical</strong></td>
<td></td>
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<td><strong>Prepregnancy evaluation</strong></td>
<td></td>
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<tr>
<td><strong>Additional evaluation for etiology of infertility</strong></td>
<td><strong>Antimüllerian hormone or basal follicle stimulating hormone plus estadiol</strong></td>
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<tr>
<td><strong>Diminished ovarian reserve</strong></td>
<td><strong>Transvaginal ultrasonography with antral follicle count</strong></td>
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<tr>
<td><strong>Ovulatory dysfunction</strong></td>
<td><strong>Ovulatory function test (eg. serum progesterone measurement)</strong></td>
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<tr>
<td><strong>Tubal factor</strong></td>
<td><strong>Hydrosalpingography</strong></td>
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<td><strong>Hydrosalpingo contrast sonography</strong></td>
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<tr>
<td><strong>Uterine factor</strong></td>
<td><strong>Transvaginal ultrasonography</strong></td>
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<td><strong>Sonohysterography</strong></td>
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<td><strong>Hysteroscopy</strong></td>
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MANAGEMENT: INFERTILITY DUE TO OVULATORY DISORDERS

If the patient is overweight or obese, lifestyle intervention should be initiated, including 5–10% weight reduction and exercise.

1. Administration of oral contraceptives
2. Administration of cyclic progestins
3. Placement of progestin intrauterine device

Administration of cosmetic therapy along with concurrent pharmacologic therapy:
- Administration of oral contraceptives
- Administration of antiandrogen therapy (with adequate contraception)
- Combination therapy

1. Preconception counseling
2. Infertility investigation
3. Administration of clomiphene or letrozole
4. Possible administration of metformin adjunct
5. Alternative ovulation induction versus in vitro fertilization

1. Administration of oral glucose tolerance test
2. Administration of metformin for evidence of impaired glucose tolerance

ACOG, Clin updates: PCOS, 2016
If weight reduction is not effective in restoring normal ovulatory function or if the patient is unable to lose weight despite adequate counseling and attempts, ovulation induction should be considered.

5-10% of body weight reduction in obese women with PCOS can restore normal ovulatory function 55-100% of women within 6 months.

Letrozole (preferred):
- started on day 3 x 5 days

Clomiphene:
- started on day 5 x 5 days

ACOG, Clin updates: PCOS, 2016
# MANAGEMENT: OTHER COMMON CAUSES OF INFERTILITY

<table>
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<tr>
<th>Etiology</th>
<th>Treatment</th>
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| Tubal factor      | **Proximal occlusion**  
|                   | *IVF first-line for all*  
|                   | • Fimbrioplasty/neosalpingostomy (distal): inferior to IVF; rates highly variable depending on extent of tubal damage  
|                   | • Salpingectomy (hydrosalpinx): preferred for hydrosalpinges, improved rates of ongoing pregnancies if done prior to IVF (OR 2.14)  
|                   | **Distal occlusion**  
|                   | **Hydrosalpinx**                                                                                                                                 |
| Endometriosis     | **Stage I-IV**  
|                   | • Surgical resection of disease, endometrioma  
|                   | • Ovulation induction, IUI, ART pending stage of endometriosis, age, response to interventions  
| Uterine factor    | **Fibroids**  
|                   | **Septa/congenital anomalies**  
|                   | **Synechiae**  
|                   | **Polyps**  
|                   | • Resect cavity-distorting fibroids (submucosal/large intramural)  
|                   | • Resect septa, adhesiolysis  
|                   | • Resect polyps (pregnancy rate 63% w/ polypectomy + IUI vs 28% w/ IUI only)  
| Male factor       | Refer to your local REI                                                                                                                                 |

**MANAGEMENT:**

- **Proximal occlusion**
- **Distal occlusion**
- **Hydrosalpinx**
- **Stage I-IV**
- **Fibroids**
- **Septa/congenital anomalies**
- **Synechiae**
- **Polyps**
- Refer to your local REI
SOCIAL DETERMINANTS OF HEALTH

Non-Hispanic Black Women:
• higher rates of tubal factor infertility, myomas, higher BMI, and later presentation for care with poorer outcomes
• Increased rates of PTB

Hispanic Women:
• significantly reduced live birth-rate

Asian Women:
• variable responses to ART treatment, suggesting biologic origins to treatment outcome disparities
• Decreased rates of PTB

All Minority Groups:
• Increased rates of moderate and severe fetal growth restriction
• Reduced odds of live birth for all three cohorts compared to the white cohort

Quinn, Fert Ster 2016

Significant disparities exist in access to infertility treatment, etiologies of infertility, and outcomes of infertility treatment between racial and ethnic groups
Description: General counseling on infertility treatment options

The patient was counseled in detail on management options for infertility. We discussed that treatment will be dependent on the etiology of her infertility after appropriate work-up. In general, we recommend optimization of health status, including 5-10% weight reduction in women with elevated BMI, exercise, and smoking cessation.

***For women with PCOS, we discussed options available, including ovulation induction with letrozole/clomiphene, gonadotropin administration, and assisted reproductive technology.
***For women with uterine polyps/septum(a), we discussed surgical optimization (i.e. polypectomy) prior further treatment.
***For women with endometriosis, we discussed management options, including ovulation induction, gonadotropin administration, ART, and surgical evaluation, including cystectomy for endometriomas.
***For women with tubal factor infertility, we discussed management options, namely ART for first-line intervention. **For women with hydrosalpinx diagnosed on imaging studies, we recommend salpingectomy prior to initiation of ART.
***For women with male factor infertility, we discussed management options and further evaluation by infertility specialists.

The patient was referred to Reproductive Endocrinology and Infertility Clinic for further evaluation, assessment, and treatment.
CODING/BILLING

ICD-10 Codes:

• N97.9 Female Infertility
• N97.0 Female infertility associated with anovulation
  • E28.2 PCOS
• N97.1 Female infertility of tubal origin
  • N701 Hydrosalpinx
• N97.2 Female infertility of uterine origin
• N80.9 Endometriosis
• Z46.9 Male infertility, unspecified
REFERENCES


• Tulandi T. Reproductive surgery for female infertility. In: UpToDate, Barbieri R (Ed), UpToDate. Waltham. MA. 2020.