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Infertility

Objectives:

- Define infertility.
- List the causes of male and female infertility.
- Describe the evaluation and initial management of an infertile couple.
- Describe the psychosocial issues associated with infertility.
- Describe management options for infertility.
- Describe ethical issues confronted by patients with infertility.
- Identify the impact of genetic screening and testing on infertility associated
- treatments.

Resources: **Kaplan Step 2 Ob/Gyn 2018, 433 Lecture.**

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❖ **Infertility:** Inability to become pregnant despite 12 months of trying to conceive without using contraception in women <35 years-old[1]. Or 6 months in women >35 years-old.

- Have a prevalence of 15% among couple.

❖ **Fecundability:** The probability of achieving a pregnancy in one menstrual cycle.

- Estimated to be 20-25% in healthy young female.
- Markedly decrease in female after the age of 38 .

❖ Factors that may contribute to infertility:

- Medical problem .
- Ethical .
- Financial .
- Psycho-social .

Who's responsible?

- **Male 20%** more common in our region than in the west.
- **Female 65%**
- **Unexplained 15%**

Male infertility	
Causes	**Detection for good sperms:**
• Male factor (30%) – decreased sperm count, decreased motility or low normal forms. • Unexplained (15%) • Unusual problems (5%)	Semen analysis[2][3]: • Abnormal > Repeat > Abnormal again? > refer to be assisted by urologist or reproductive endocrinologist.

[1] 85% of couples achieve pregnancy after 12 consecutive months
[2] Obtained by masturbation after 2-3 days of abstinence.
[3] Volume, concentration, motility and morphology.

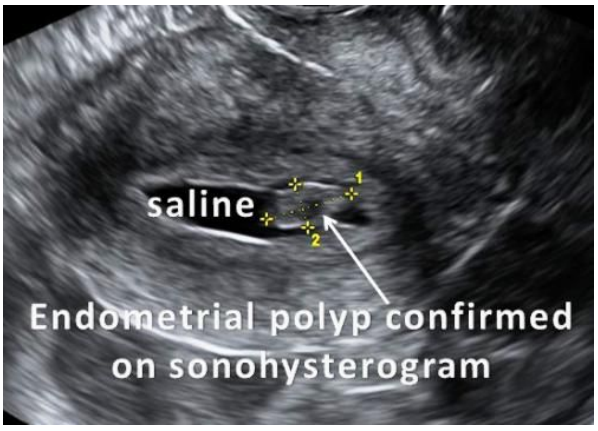
Female infertility	
Causes	**Detection for good oocyte:**

• **Ovulatory dysfunction** (20%) – anovulation due to:
  ○ PCOS, Thyroid disorders, age and hyperprolactinemia.
• **Tubal and pelvic** (30%)
  ○ Endometriosis, pelvic adhesions, pelvic inflammatory diseases and abdominal or pelvic surgeries
• **Unusual problems** (5%) – Uterine anomalies but in case of: Abnormal bleeding, pregnancy loss, preterm delivery, previous uterine surgery. Uterine assessment must be done.
• **Unexplained** (15%).
	• **History of regular menses** suggest ovulatory cycles.
	• **Ovulation predictor kit**: To asses ovulation based on the increase LH production which can be detected by urine.
	• Basal body temperature charting: Women can monitor her ovulation by checking her daily body temperature which is the effect of high levels of progesterone during the luteal phase of the cycle.

They may ask you in the MCQs or the OSCE about the female & male causes of infertility.

❖ Evaluation of an infertile couple: (investigation)

- TSH level .
- Prolactin 60 ng/ml (normal range <20 ng/ml).
- Progesterone (course of 21 days).
- Hysterosalpingogram (HSG): demonstrate a normal uterine cavity with spill of radiopaque dye from both fallopian tube. **May come in OSCE.**
- Saline infusion sonohysterography (SIS): same as HSG but with the advantage of using ultrasound, can be done at the clinic and Avoiding the use of dye.
- Semen analysis with with 2ml of semen (normal >1.5), 4 million sperm/ml (normal > 15), 20% motility (normal >40%), 2% normal morphology (normal >4%)
- Discussion regarding frequency and timing of intercourse.
- Ovarian reserve testing: Day 3 FSH 8.3 mIU/ml, estradiol <20 pg/ml, antimullerian hormone (AMH) 1.1 ng/ml which are considered normal.



SIS

HSG

❖ Initial management of an infertile couple: MCQ or OSCE!

1- Ovarian stimulation.

2- Assisted reproductive technologies.

1- Ovarian stimulation		
Clomiphene citrate	**Purified gonadotropins**	**Intrauterine insemination**
Selective estrogen receptor modulator. - Stimulate ovaries to increase follicular development. -10% risk of multiple gestation	Stimulate ovaries to increase follicular development. -25% risk of multiple gestations.	Ejaculated semen is washed and introduced to uterine cavity by a catheter.

2- Assisted reproductive technologies

In vitro fertilization: 30% risk of multiple gestation.

- **Indications:**

1- Blocked or absent fallopian tubes .
2- History of tubal sterilization.
3- Sever pelvic adhesions.
4- Sever endometriosis.
5- Poor ovarian response to stimulation.
6- Severe male factor infertility.
7- Failed treatment with less aggressive therapies.

- **Pre-implantation genetic diagnosis:** Genetic profiling of embryo prior to implantation; if the couple know that they are carriers of any inherited disease such as: cystic fibrosis or tay-sachs disease embryo can be tested for this prior implantation.

- **Psycho-social stress:** Social support that patients receive can have significant effect in stress level. Compared to white & Asian women black women are less likely to report encouragement for treatment from their partners & family members.

Case

A 37-year-old woman and her 37-year-old male partner present with the complaint of a possible fertility problem. The couple has been married for 2 years. The patient has a 4-year-old daughter from a previous relationship. The patient used birth control pills until one-and-a- half years ago. The couple has been trying to conceive since then and report a high degree of stress related to their lack of success. The patient reports good health and no problems in conceiving her previous pregnancy or in the vaginal delivery of her daughter who has cystic fibrosis. She reports that her periods were regular on the birth control pill, but have been irregular since she discontinued taking them. She reports having periods every 5-7 weeks. She works as a cashier, runs 12-24 miles each week for the last 2 years, and has no history of STIs, abnormal Paps, smoking, alcohol or other drugs. She has had no surgery. She has been taking a multivitamin with folic acid since trying to conceive.

The patient's partner also reports good health and reports no problems with erection, ejaculation or pain with intercourse. He has had no prior urogenital infections or exposure to sexually transmitted infections. He has had unprotected sex prior to his current relationship, but has not knowingly conceived. He has no medical problems or past surgery. The couple has vaginal intercourse 3-5 times per week when he is at home.

The female patient is 5'9" and weighs 130 pounds. Head and neck examination is unremarkable. Specifically there is no evidence of thyromegaly. Breast exam reveals no tenderness or masses, but she has bilateral galactorrhea on compression of the areola. Pelvic exam reveals normal genitalia, well-estrogenized vaginal mucosa and cervical mucus consistent with the proliferative phase. The uterus is anteflexed and normal in size without masses or tenderness. Several tests were ordered.

1- What is the definition of infertility?

Inability to become pregnant despite 12 months of trying to conceive without using contraception in women <35-years-old.

Six months of unprotected intercourse defines infertility in women 35 years and older. About 15% of couples experience this problem.

2- What are the etiologies of infertility?

- Ovulatory dysfunction (20%) - anovulation.
- Male factor (30%) – decreased sperm count, decreased motility or low normal forms (morphology).
- Tubal and pelvic (30%) – tubal damage due to pelvic infection, or pelvic factors such as endometriosis or pelvic adhesions.
- Unexplained (15%).
- Unusual problems (5%).

3- What is the initial work-up for infertile couples and what tests would you add for this particular couple?

- Normal TSH.
- Prolactin 60 ng/ml (normal range < 20 ng/ml).
- Evaluation for ovulation: Progesterone (day 21) was 1.2 ng/ml (≥ 3 ng/ml will indicate ovulation).
- Could also review basal body temperature charting or have patient use ovulation predictor kits.
- Hysterosalpingogram demonstrated a normal uterine cavity with spill of radiopaque dye from both fallopian tubes.
- Semen analysis with 2ml of semen (normal >1.5), 4 million sperm/ml (normal >15), 20% motility (normal >40%), 2% normal morphology (normal >4%).
- Discussion regarding frequency and timing of intercourse.
- Ovarian reserve testing: Day 3 FSH 8.3 mIU/ml, estradiol <20 pg/ml, antimullerian hormone (AMH) 1.1 ng/ml which are considered normal.

4- Offer genetic counseling and testing for cystic fibrosis mutations. Given the results of the tests, what is the differential diagnosis for the etiology(ies) of this couple's infertility?

- Anovulation secondary to hyperprolactinemia from a potential prolactinoma
- Oligospermia – repeat semen analysis once and consider referral to a urologist.

5- What is the appropriate management for etiology of this couple's infertility?

- For anovulation secondary to a possible prolactinoma, the patient should have a head MRI to rule out a pituitary lesion. Treat with bromocriptine to lower prolactin levels, which will usually result in regular ovulation.
- If she remains anovulatory after management of her prolactinoma with bromocriptine to normalize her prolactin level, ovulation induction may be offered with clomiphene citrate.
- For oligospermia, refer to a urologist for evaluation for correctable causes. However, if oligospermia remains after evaluation and treatment then options include in vitro fertilization with intracytoplasmic sperm injection, intrauterine insemination with partner's sperm, intrauterine insemination with donor sperm, adoption.

6- The husband elects to undergo testing for common cystic fibrosis mutations and is determined to be a carrier. What options are available to them to achieve a pregnancy that is less likely to lead to a child affected by cystic fibrosis? Discuss the ethical issues associated with these choices.

- The couple could elect to use donor sperm or donor eggs. In both cases one of the parents would not be genetic parents.
- The couple could elect to use IVF with preimplantation genetic diagnosis.
- The couple could elect to achieve a pregnancy with none of the above techniques and accept a 1:4 risk of having a child affected with CF. They could elect to undergo antepartum testing (chorionic villi sampling, amniocentesis, etc.) to determine if the pregnancy is affected with CF.