

INFERTILITY

By Jessica Boone MPA, PA-C

Basic Infertility Evaluation &
Treatment Options

Objectives

After participating in this presentation, the PA will be able to:

- Recognize the causes of infertility
- Outline the basic tenets for an infertility evaluation
- Define the treatment modalities for an infertile patient

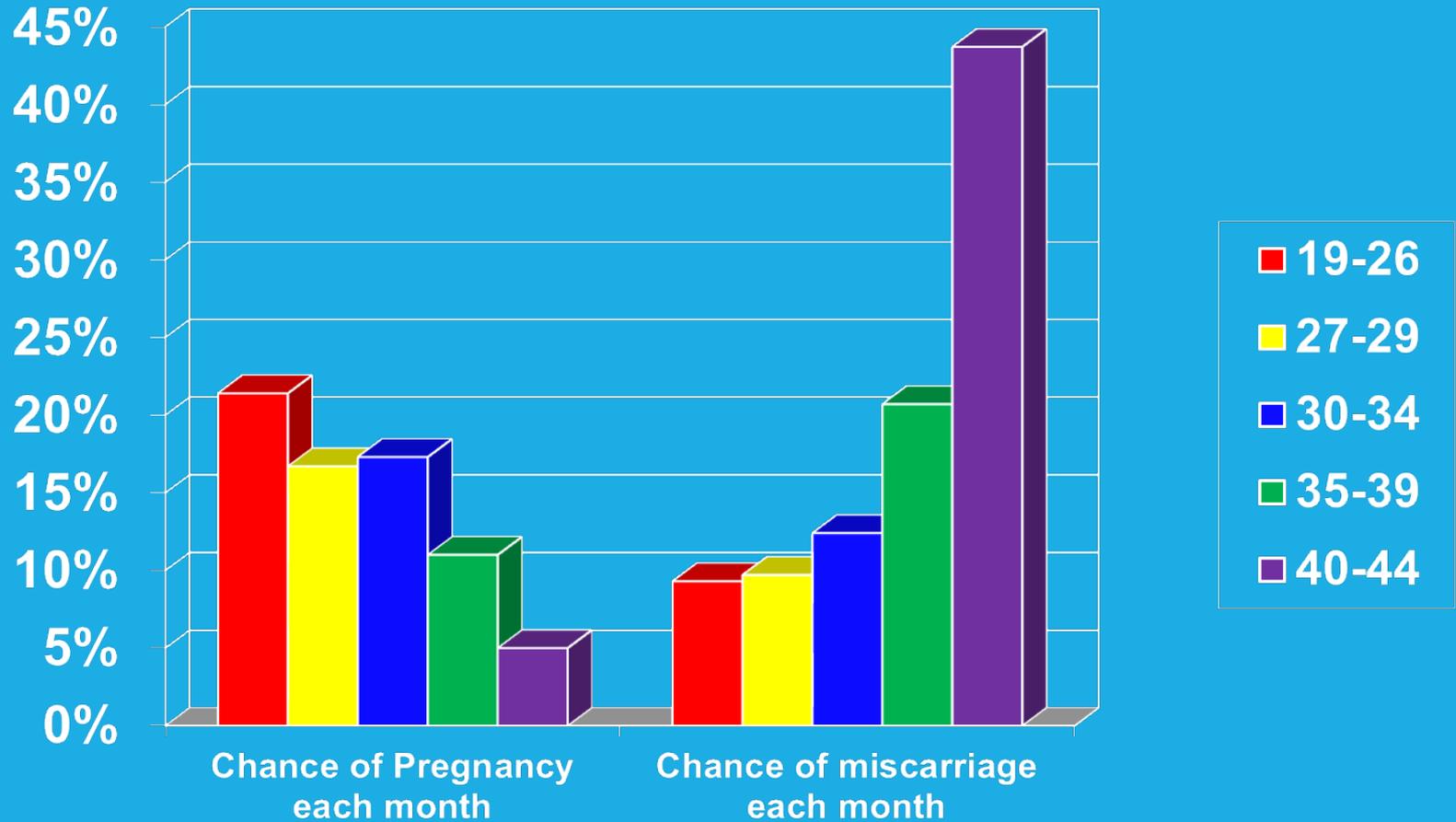
Myths

- It should be easy to get pregnant

Facts

- Prior to age 32 approximately 20% chance of pregnancy per month
- Egg quality decreases at the age of 32
- After age 35 approximately 10% chance of pregnancy per month
- Approximately 15 - 20% chance of ALL pregnancies will result in miscarriage.
 - This probability increases with age

Pregnancy Success Rates



Myths

- Miscarriages are caused by:
 - Stress
 - Picking up something heavy
 - Having intercourse
 - Exercise

Facts

- Miscarriages are usually the result of genetically abnormal egg and/or sperm resulting in a genetically abnormal embryo
 - Especially miscarriages that occur in the 1st trimester
- This cannot be prevented once the embryo has formed

Myths

- Most people who get pregnant at fertility clinics, have “multiples” (twins, triplets and more)

Facts

- ~ 80% patients who conceive at a fertility clinic have a singleton pregnancy
- 10 - 20% will have twins
- <1% of all patients have triplets
- Most multiples pregnancy are conceived with ovulation induction/IUI and not IVF

Myths

- Insurance never covers the cost of infertility treatment

Facts

- 56% of employers will cover some portion (evaluation, medications or treatment)
- As of 4/2021, 19 states already have laws mandating fertility coverage with 13 of those states requiring coverage for IVF
 - Colorado Building Families Act was passed 4/1/20 and was supposed to take effect 1/1/22, but the bill stalled.

Myths

- If I go through IVF or IUI treatment I will go into menopause early

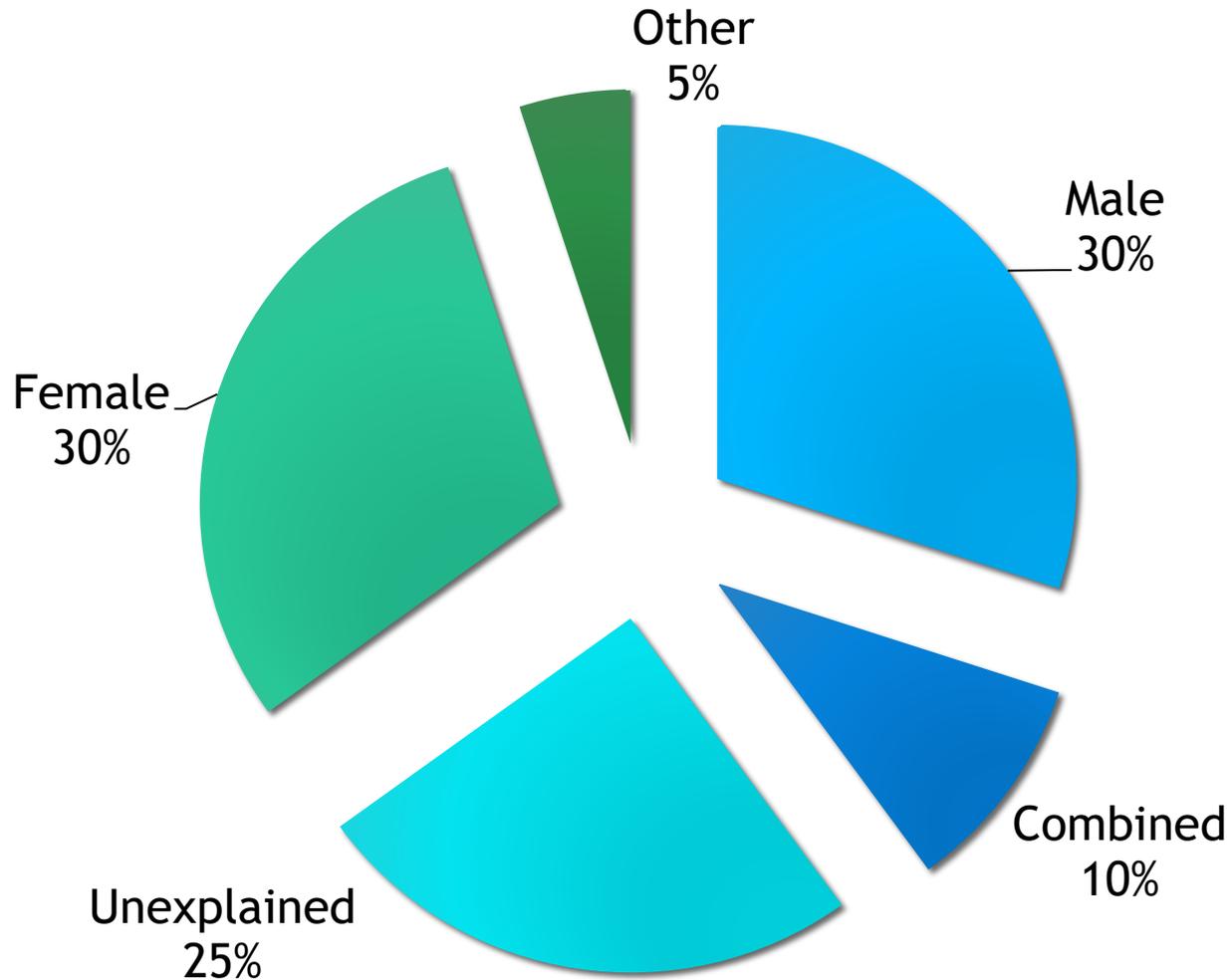
Facts

- Studies show no impact on long term fertility or menopause
- Every month there is a cohort of eggs competing to be the one egg to ovulate and hopefully cause pregnancy.
- The eggs that do not “win” the competition undergo atresia and never ovulate. A new cohort of eggs compete the following month.
- Fertility treatments are simply taking advantage of the eggs that would normally be lost to atresia

Infertility

- Definition: one year of unprotected intercourse without conception
 - 85% of couples conceive in the first year
- Worldwide, 1 in 7 couples have problems conceiving (15%)
- Primary Infertility: when a couple has been unable to conceive after one year of unprotected intercourse
- Secondary Infertility: inability to become pregnant after previously giving birth to a baby

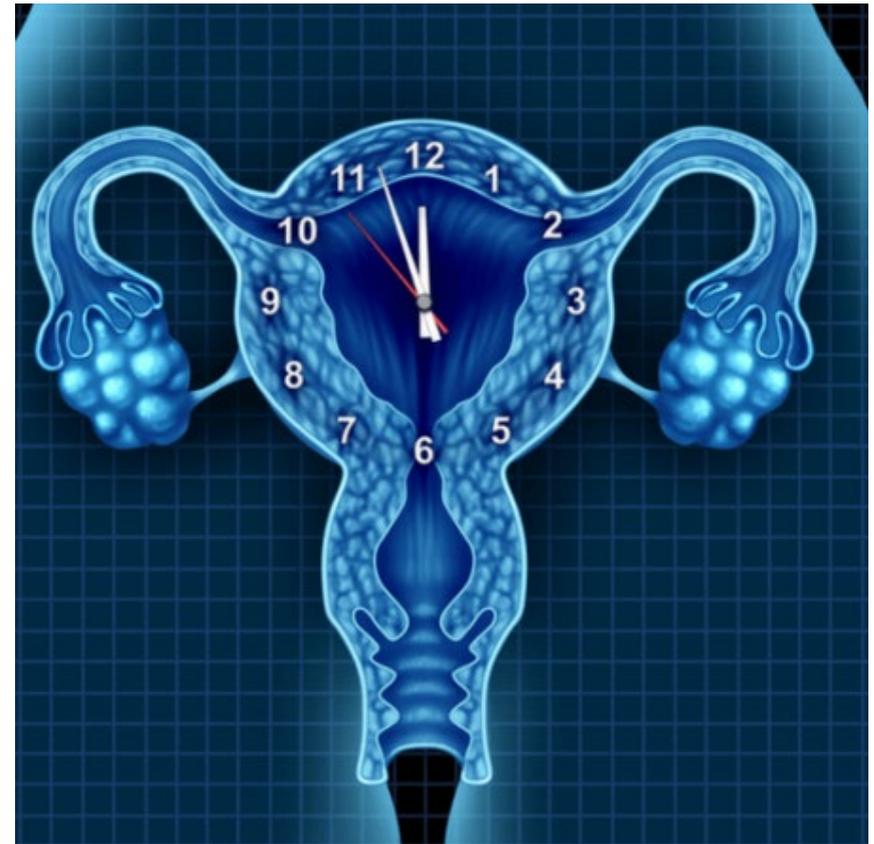
Causes of Infertility



Causes of Female Infertility

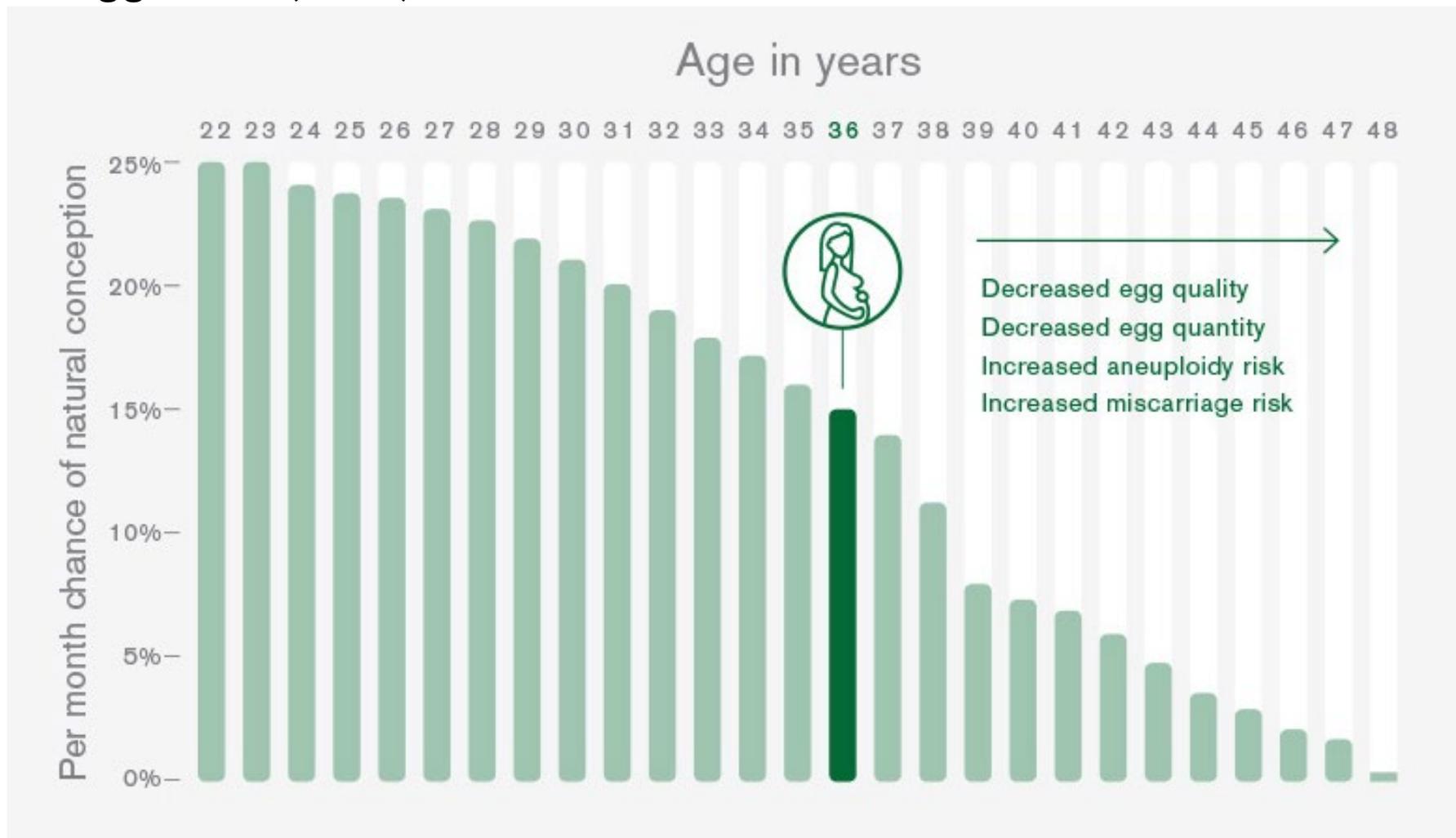
Causes of Female Infertility

- Egg factor (50%)
 - Age
 - Ovarian reserve
- Anovulation (25%)
 - Hormonal problems
 - Damage to ovary
 - Premature ovarian insufficiency
- Anatomic (25%)
 - Blocked or diseased fallopian tubes
 - Abnormality of the uterus
 - Abnormality of the cervix



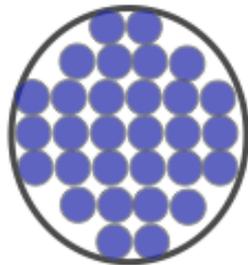
Causes of Female Infertility: Age

- **Egg factor (50%)**

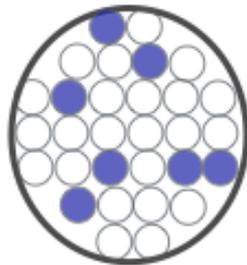


Causes of Female Infertility: Ovarian Reserve

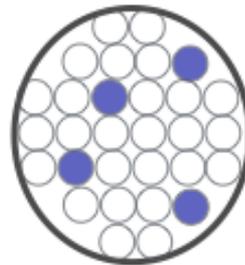
- Egg factor (50%)
 - Age
 - **Ovarian reserve**
 - 1-2 million eggs at birth
 - Approximately 300,000 eggs at puberty
 - About 300 oocytes are ovulated over reproductive years
 - 25,000 eggs at age 37-38
 - <1000 eggs at menopause



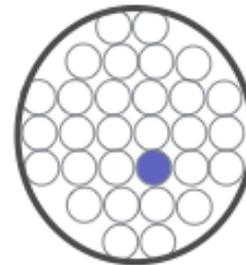
Birth
1-2 million eggs



Puberty
300-500,000 eggs

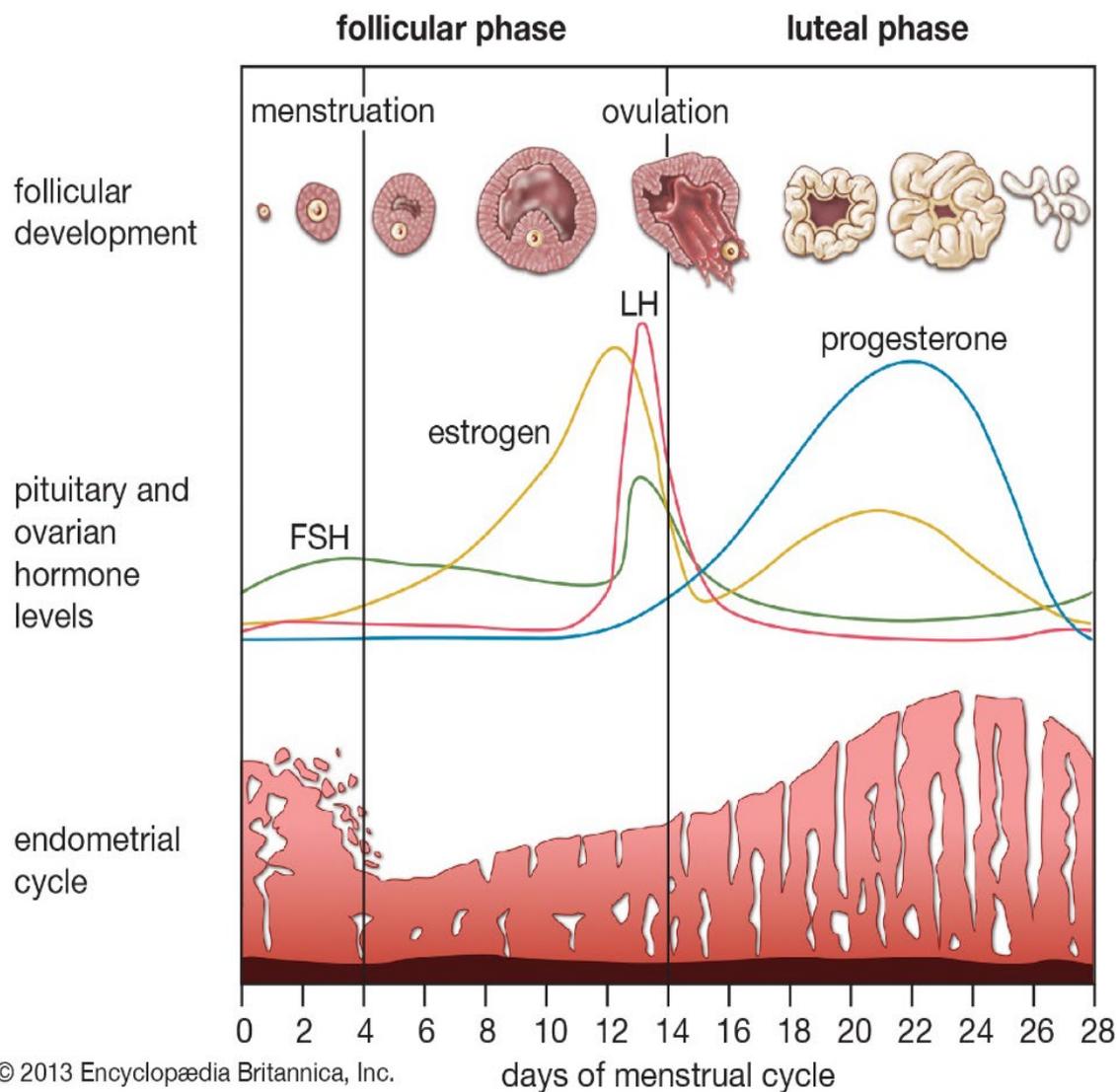


Age 30
180,000 eggs



Age 51
1,000 eggs

Causes of Female Infertility: Ovarian Reserve



Cycle Length: 25 – 36 days

Phase 1: Follicular (varies)

Phase 2: Ovulatory

Phase 3: Luteal (14 days)

Follicular Stimulating Hormone (FSH): released by anterior pituitary; causes growth of follicle

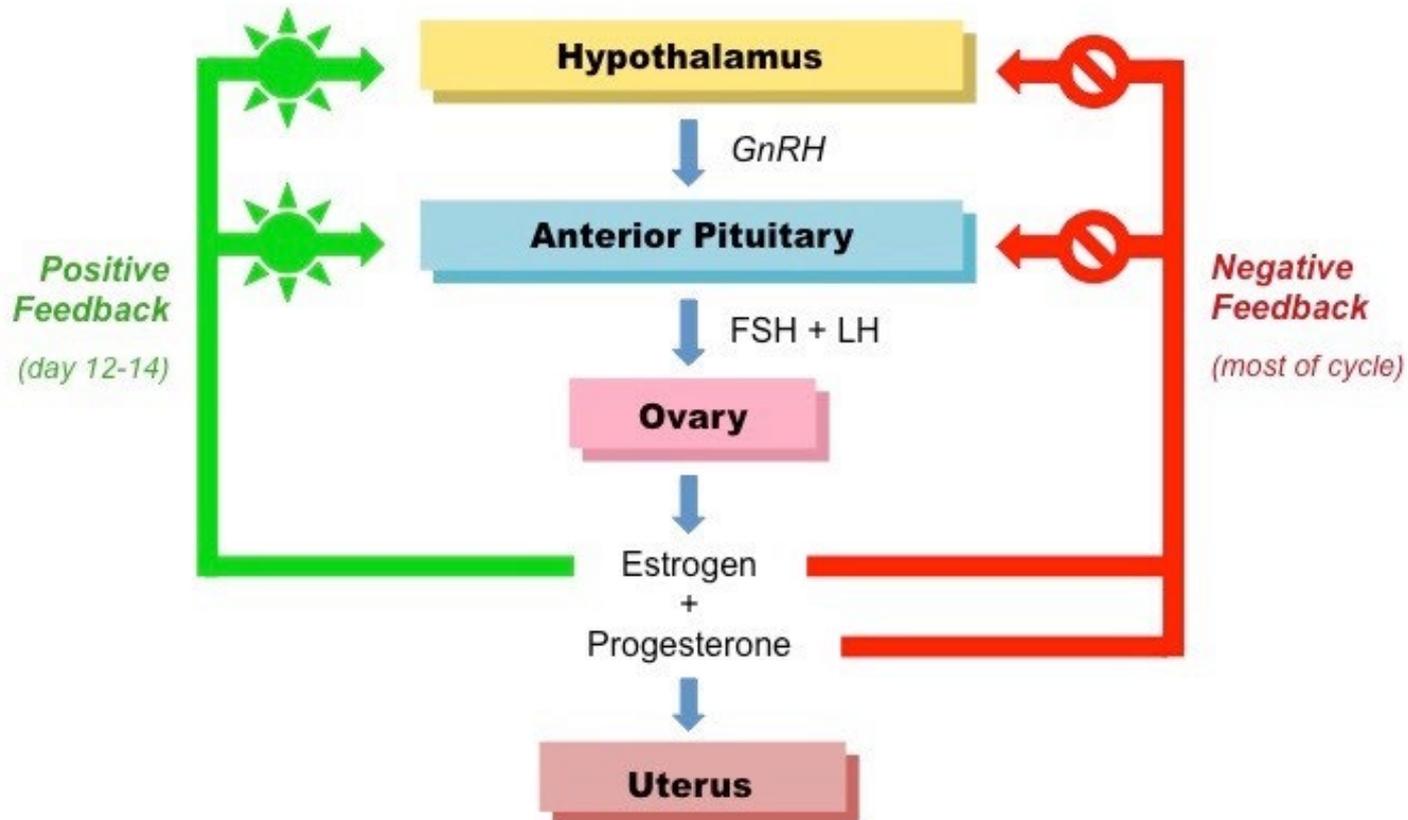
Estrogen/Estradiol (E2): released by the growing follicle; thickens endometrial lining

Luteinizing hormone (LH): released by anterior pituitary; triggers ovulation.

Progesterone (P4): released by corpus luteum, supports pregnancy

Causes of Female Infertility: Ovarian Reserve

The Hypothalamic Pituitary Axis



Causes of Female Infertility: Ovarian Reserve

- Egg factor (50%)
 - Age
 - Ovarian Reserve
 - 1-2 million eggs at birth
 - Approximately 300,000 eggs at puberty
 - 25,000 eggs at age 37-38
 - <1000 eggs at menopause
 - **Diagnosis:**
 - Quality check: Day 3 FSH and Estradiol
 - Quantity check: Anti-Mullerian Hormone (AMH)

Hormone	Ideal	Borderline	Elevated
FSH	< 9.0	9.0 -12.0	> 12.0
E2	< 50	50-75	> 75

***** You cannot interpret the FSH level without the Estradiol. Always order both!*****

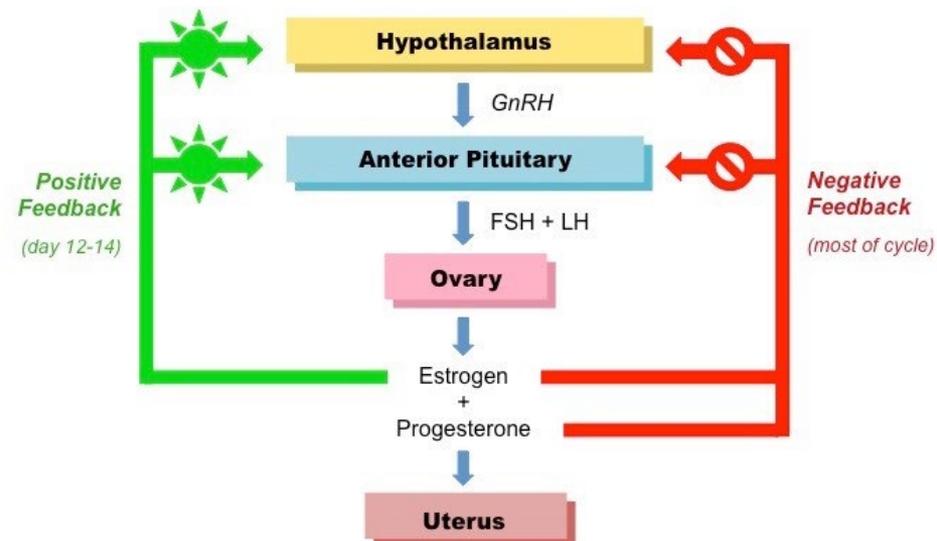
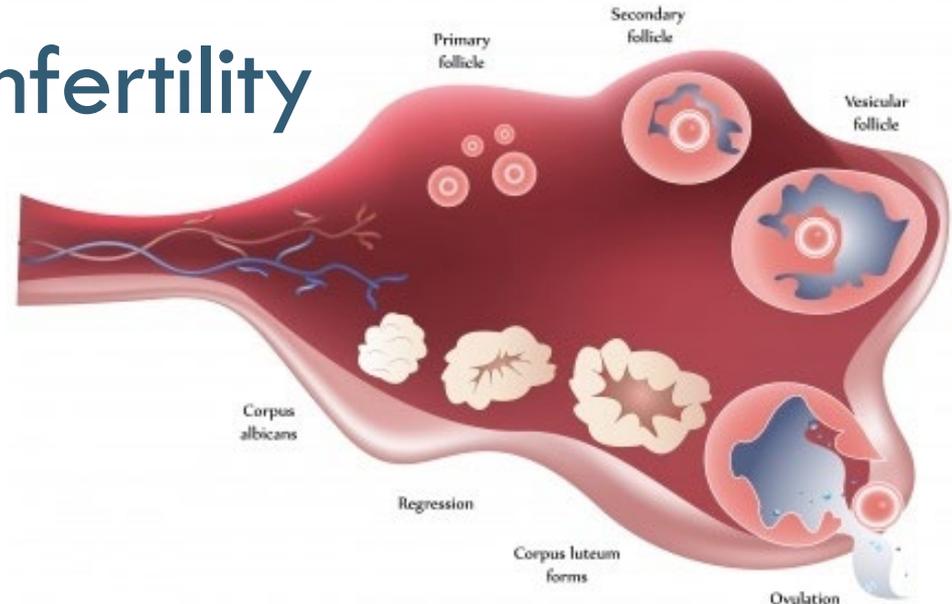
Serum AMH Level Distribution (ng/mL)

Age (yr)	5 th %	10 th %	Median	90 th %	95 th %
25	1.56	2.01	5.42	10.64	13.87
30	0.72	1.16	3.53	8.35	11.02
32	0.48	0.88	3.44	7.86	10.19
34	0.42	0.65	2.49	6.57	7.62
36	0.31	0.50	2.28	5.95	8.62
38	0.15	0.32	1.66	5.20	6.66
40	0.09	0.29	1.27	3.73	5.78
42	0.07	0.17	1.20	3.67	4.31
>43	0.00	0.00	0.72	2.49	2.87
All	0.30	0.62	2.91	8.30	10.93

****AMH does not predict your ability to conceive, it is simply an indicator of your ovarian reserve. This is especially important for those patients who have never tried to conceive.****

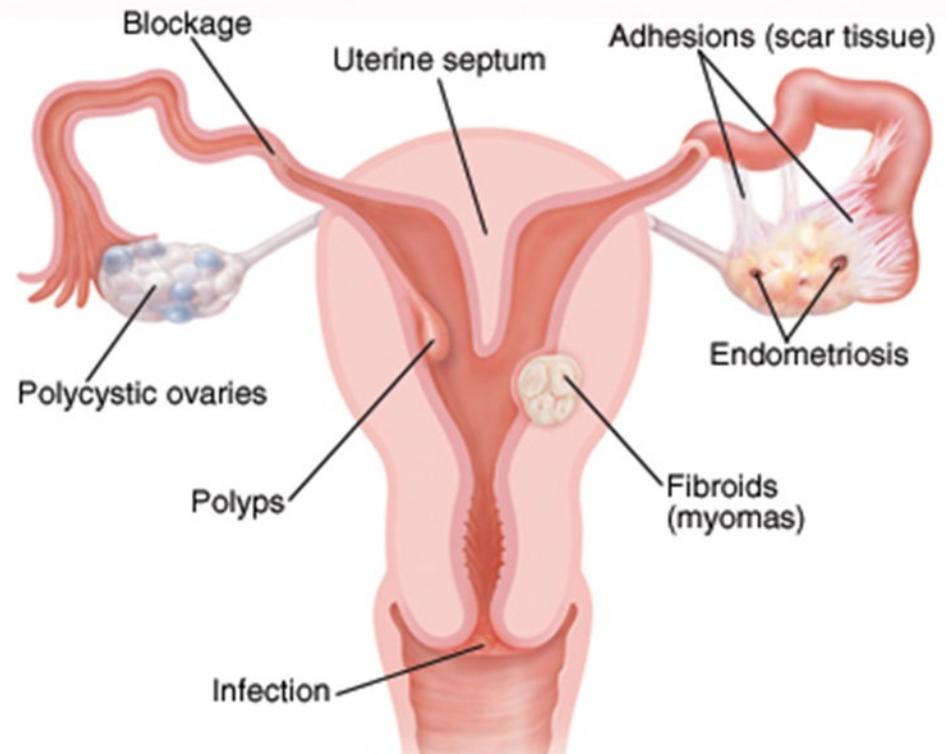
Causes of Female Infertility

- Egg factor (50%)
- **Anovulation (25%)**
 - Hormonal problems
 - Polycystic Ovarian Syndrome (PCOS):
 - Ovaries fail to produce a normal follicle → infrequent ovulation and/or immature egg
 - Malfunction of the hypothalamus
 - Malfunction of the pituitary gland
 - Damage to ovary (ex: surgery or endometriosis)
 - Premature ovarian insufficiency



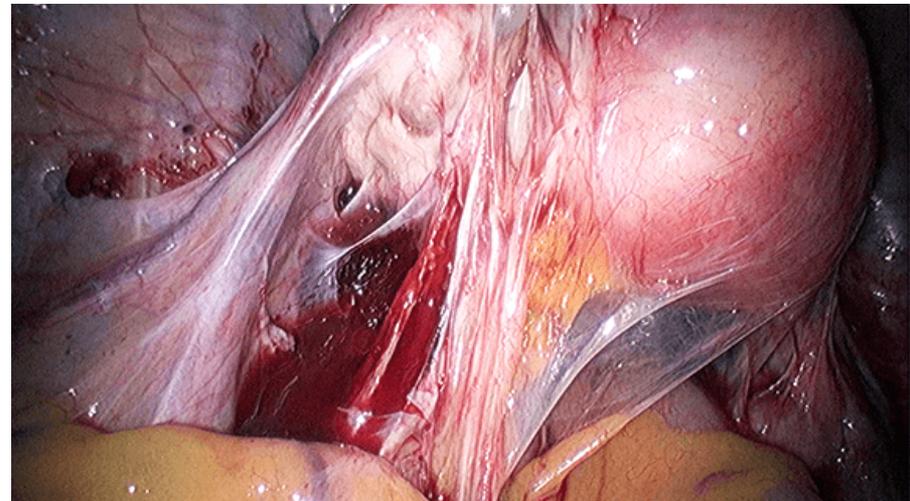
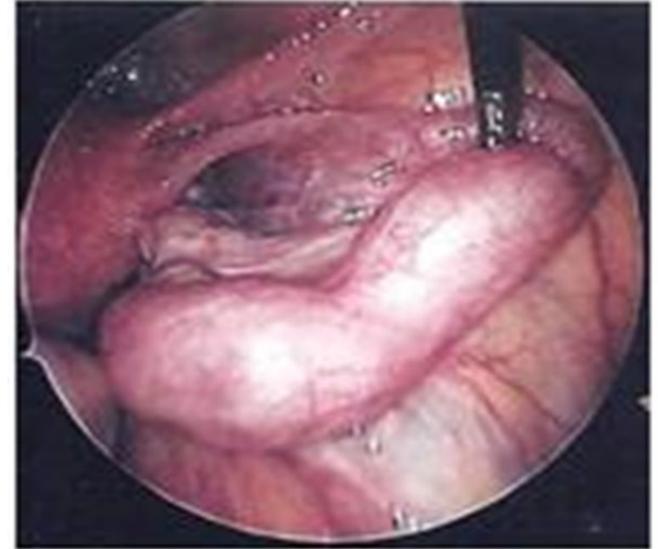
Causes of Female Infertility

- Egg factor (50%)
- Ovulation (25%)
- **Anatomic (25%)**
 - Blocked or diseased fallopian tubes
 - Endometriosis
 - Abnormality of the uterus
 - Abnormality of the cervix

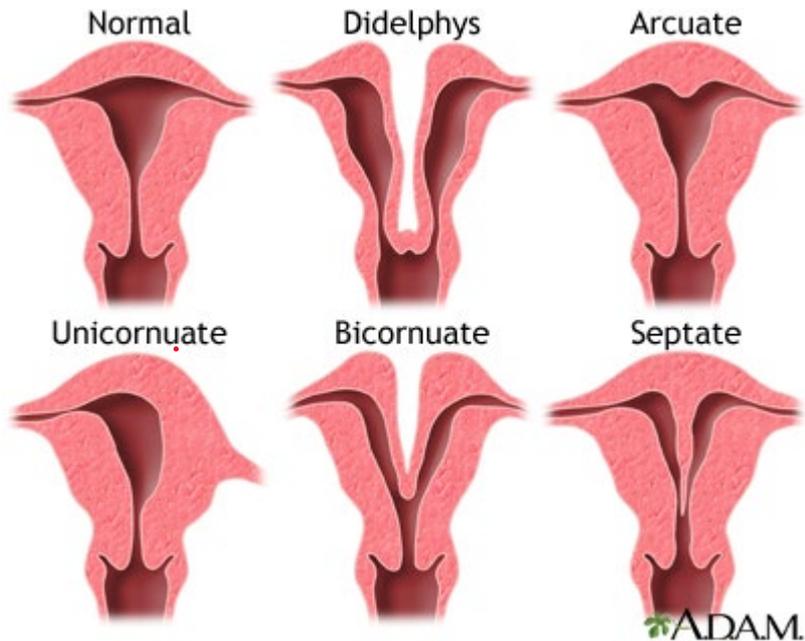


Causes of Female Infertility: Tubal Disease

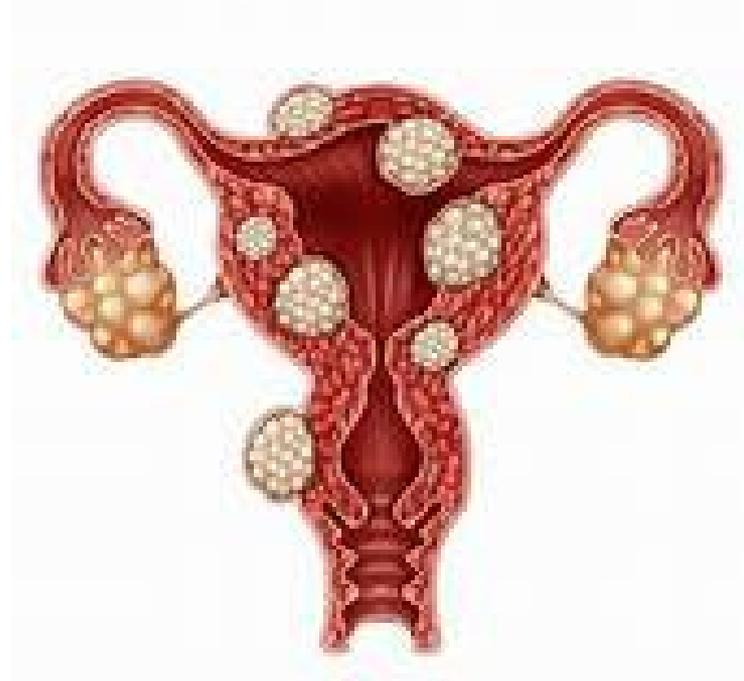
- Tubal disease affects approximately 25% of infertile couples
- Main causes:
 - Infection (ex: Chlamydia)
 - Abdominal/Pelvic disease
 - appendicitis, colitis, surgery
 - endometriosis
 - Ectopic pregnancy



Causes of Female Infertility: Uterine Anomalies



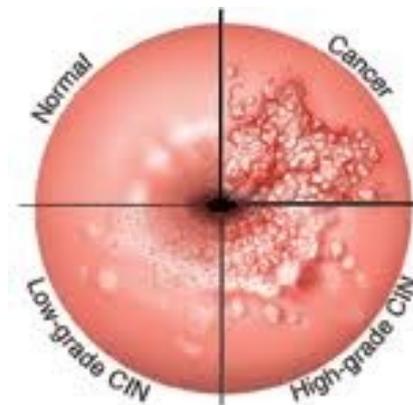
Possible uterine abnormalities include scar tissue, endometrial polyps (bunched-up pieces of the endometrial lining), fibroids (over growth of uterine muscle), or an abnormally-shaped uterine cavity.



Congenital abnormalities, such as septate uterus, may lead to recurrent miscarriages or the inability to conceive.

Causes of Female Infertility: Cervical Factor

- 3% of couples face infertility due to a cervical mucus factor
- Treatment of cervical intraepithelial neoplasia (CIN) (ex: LEEP)
 - Stenosis
 - Increased risk of 2nd trimester miscarriage and preterm labor



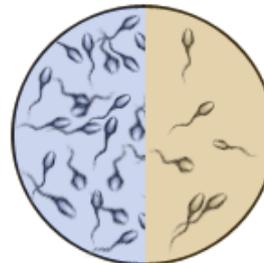
Causes of Male Infertility

Causes of Male Infertility

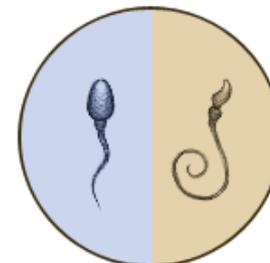
- **Poor semen quality**

Semen Analysis	Lower Reference Limit
Semen Volume	1.5mL
Sperm Concentration	15 million/mL
Sperm Motility (Progressive)	32%
Total Sperm Motility (Progressive and Nonprogressive)	40%
Total Sperm Count	39 million
Morphology	4%

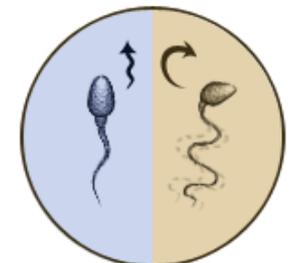
Normal sperm count Low sperm count Normal sperm Abnormal sperm Normal forward progression Abnormal motility



Sperm count



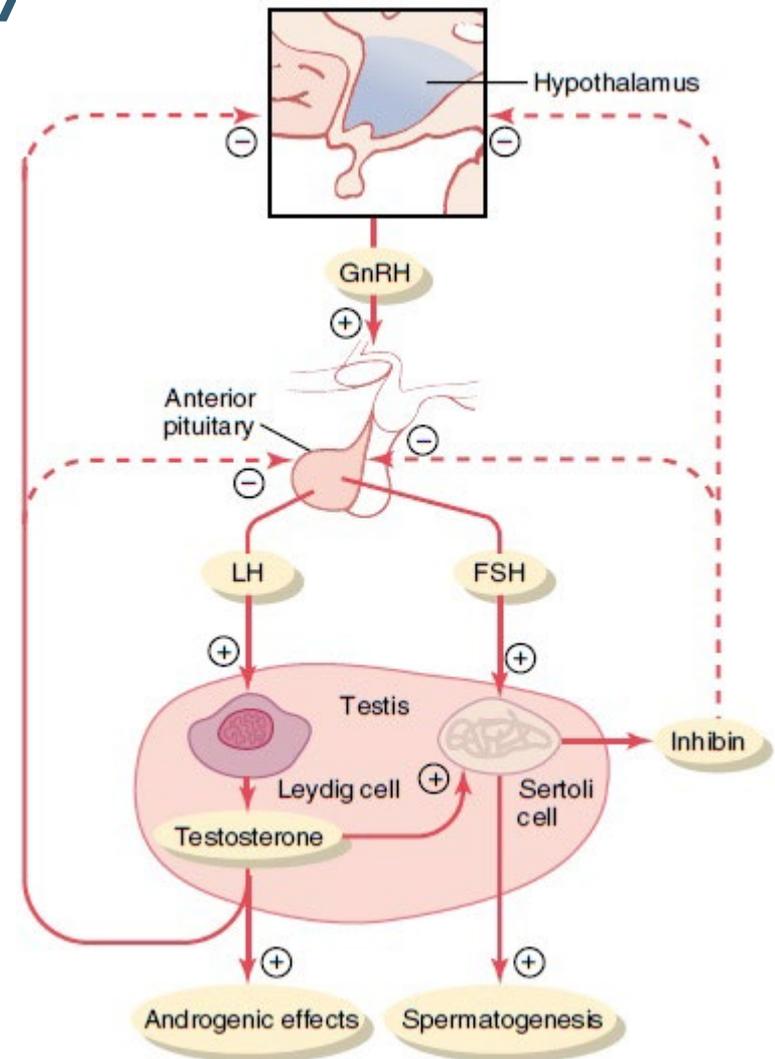
Sperm morphology



Sperm motility

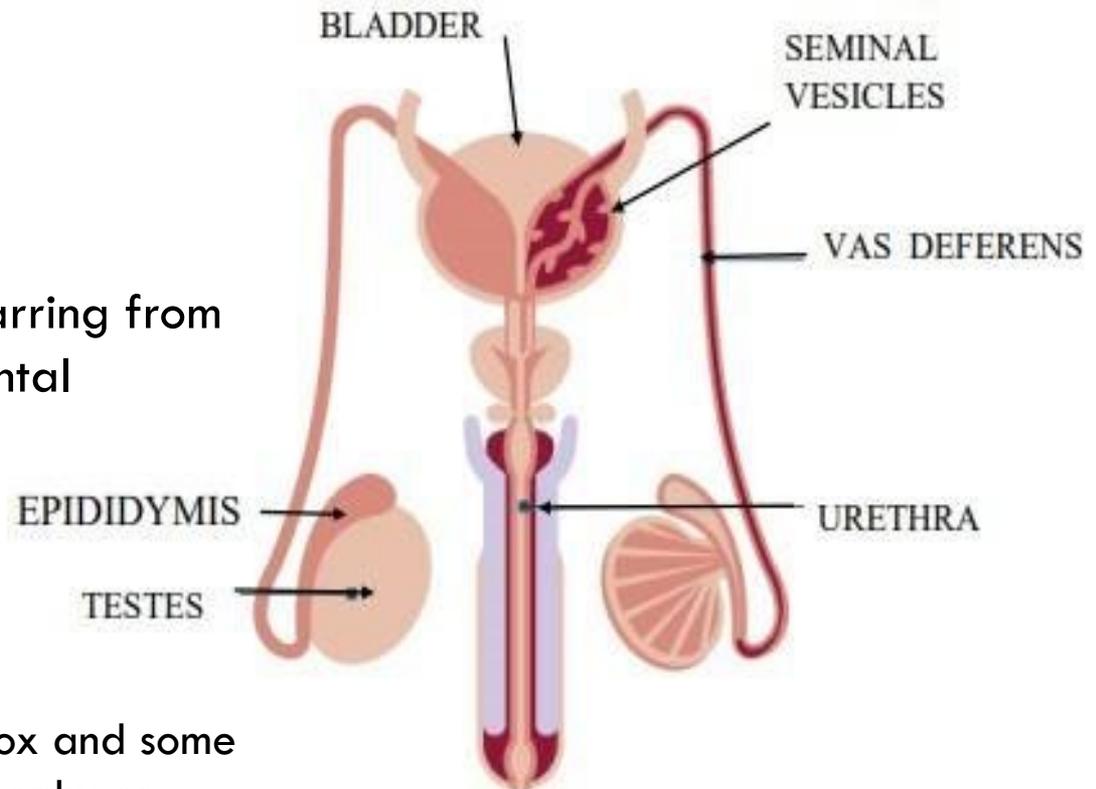
Causes of Male Infertility

- Poor semen quality
- **Hormonal Problems**
 - Failure to release GnRH properly → lack of testosterone → no sperm
 - Failure to release LH/FSH from pituitary → lack of testosterone → decrease in sperm
 - Leydig cells are unresponsive to LH stimulation → no testosterone production → no sperm
 - No testosterone = No sperm



Causes of Male Infertility

- Poor semen quality
- Hormonal Problems
- **Anatomical problems**
 - Varicocele
 - Damaged vas deferens (scarring from infection, elective or accidental vasectomy, genetics)
 - Testicular Torsion
 - Retrograde ejaculation
 - Infection/Disease
 - Mumps, tuberculosis, smallpox and some STI's can cause testicular atrophy or damage



Causes of Male Infertility

- Poor semen quality
- Hormonal Problems
- Anatomical Problems
- **Psychological/Physical Problems**
 - Erectile dysfunction
 - Premature ejaculation
- **Environmental Factors**
 - Smoking – quit 3 months prior to trying to conceive!
 - Prolonged use of marijuana and/or recreational drugs
 - Chronic alcohol abuse
 - Anabolic steroid use
 - Overly intense exercise
 - Tight underwear

Basic Infertility Evaluation

When to Begin Basic Evaluation

- After 1 year of unprotected intercourse
- After 6 months for women > 35 years old
- As soon as pregnancy is desired if
 - Known problem such as infrequent or absent menstrual cycles
 - Know or suspected tubal disease
 - Know history of infertility for patient or partner



Female Infertility Evaluation

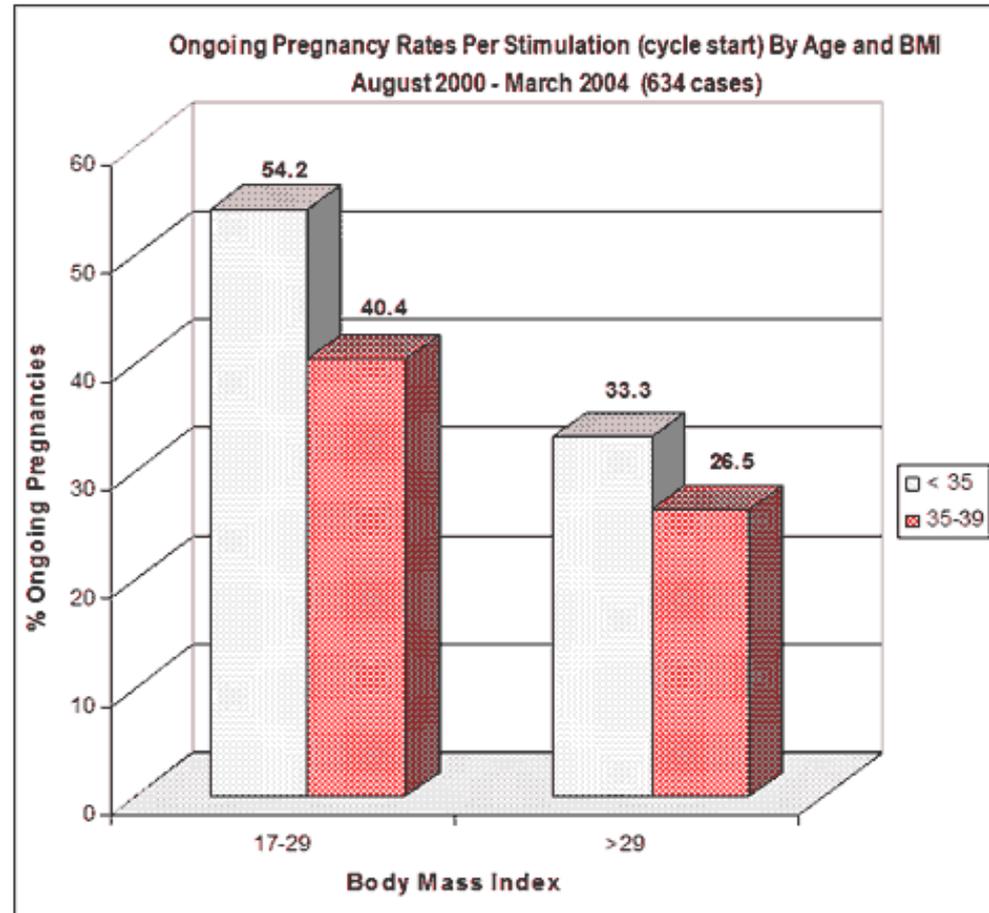
- **Medical History**

- Duration of infertility
- Sexual history
 - Coital frequency and sexual dysfunction
- Prior infertility evaluation and treatment
- Pregnancy history
- Gynecologic history
 - Menstrual pattern and presence of menstrual cramps
 - History of STIs or abnormal PAP smear
 - Prior pelvic surgery: cervix, uterus, ovaries, appendix
- Medical and surgical history
- Medications and social habits
 - Smoking- accelerates egg loss, ↑ the risk of SAB, preterm birth, and low birth weight. Quit 2 – 3 months prior to trying to conceive or treatment!
- Family history: infertility, age of menopause, genetic disease
- What is the ultimate family planning goal?



Female Infertility Evaluation

- Medical History
- **Focused physical exam**
 - Signs of androgen excess or insulin resistance ...think PCOS (ex: acne, hirsutism, acanthosis nigricans)
 - BMI (ideal if <30)
 - Elevated BMI associated with ↓ fertility, ↑ risk of miscarriage, and lower ongoing pregnancy rate
 - 10% weight loss over 3 months



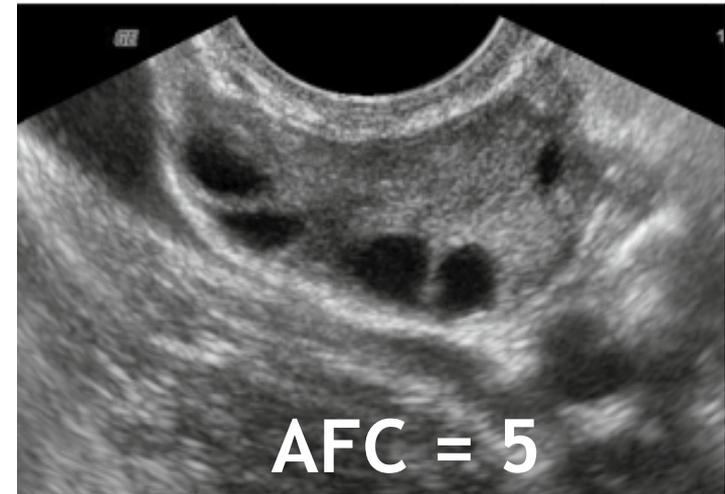
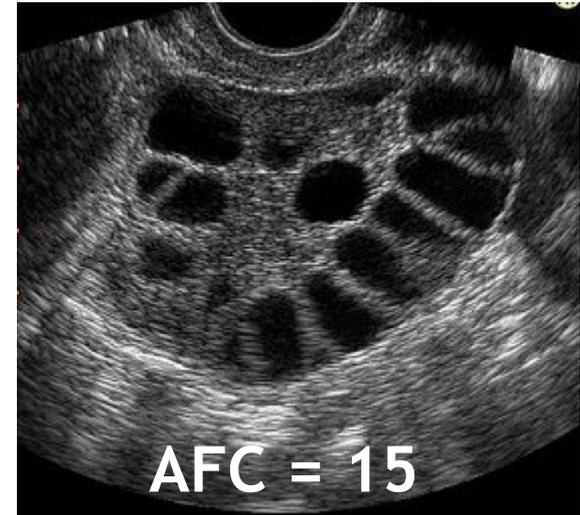
Female Infertility Evaluation

- Medical History
- Focused physical exam
- **Ovulation Detection**
 - Menstrual history
 - Mollimina symptoms: breast tenderness, bloating, cramping, emotional changes
 - Ovulation predictor kit starting cycle day 8
 - Progesterone blood work 7 days after LH surge



Female Infertility Evaluation

- Medical History
- Focused physical exam
- Ovulation detection
- **Pelvic ultrasound to assess antral follicle count (AFC)**
 - Will always be performed by the reproductive endocrinologist
 - Easiest to visualize antral follicles in early follicular phase, but can be performed at any point in the cycle
 - Normal AFC is 5 – 9 per ovary or total AFC of 10 -18
 - PCOS > 12 per ovary
 - Can also assess for fibroids or abnormal shape to uterus



Female Infertility Evaluation

- Medical History
- Focused physical exam
- Ovulation Detection
- Pelvic ultrasound
- **Laboratory Evaluation**
 - Quality check: Day 3 FSH/Estradiol
 - Quantity check: AMH
 - Progesterone day 7 after LH surge
 - Thyroid Function Studies
 - Prolactin
 - Vitamin D
 - Preconception Panel: Blood type, antibody screen, Varicella IgG, Rubella IgG
 - Infectious disease testing typically needs to be current within past year for fertility treatments
 - Recessive carrier genetic screening



Female Infertility Evaluation

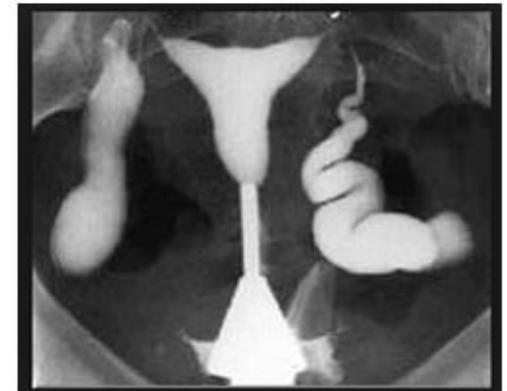
- Medical History
- Focused physical exam
- Ovulation Detection
- Pelvic ultrasound
- Laboratory Evaluation
- **Anatomic evaluation to assess uterus and fallopian tubes**
 - **Sonohysterogram with tubal evaluation (Femvue) or Hysterosalpingogram (HSG)**



NORMAL HSG



BLOCKED TUBES



HYDROSALPINX

Male Infertility Evaluation

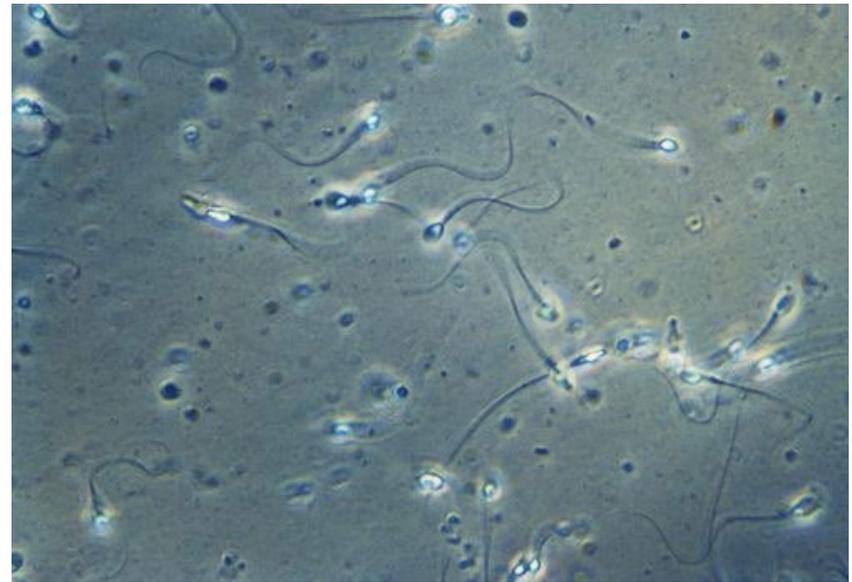
• Medical History

- Prior paternity
- Prior infertility/urologic evaluation
- Genitourinary history
 - Injury, undescended testes, varicocele
- Medical and surgical history
- Medications and social habits
- Family history of infertility, genetic disease
- Any history of sexual dysfunction
- Exposure to reproductive toxins



Male Infertility Evaluation

- Medical History
- **Semen Analysis**
 - Recommendations: 2 – 7 days abstinence, avoid lubricants, sample to the lab within 1 hour of collection
 - General: volume, liquefaction, consistency, pH
 - Microscope: count, motility, morphology, agglutination, foreign bodies (ex: bacteria)
- **Focused physical exam with urologist**



What is helpful to complete before referral to a reproductive endocrinologist?

Female

- Medical History
- Focused physical exam
- **Ovulation Detection**
- Pelvic ultrasound
- **Laboratory Evaluation**
 - Quality check: Day 3 FSH/Estradiol
 - Quantity check: AMH
 - Progesterone day 7 after LH surge
 - Thyroid Function Studies
- **Anatomic evaluation**

Male

- Medical History
- **Semen Analysis**
- Focused physical exam

Treatment of Infertility

Treatment Of Infertility

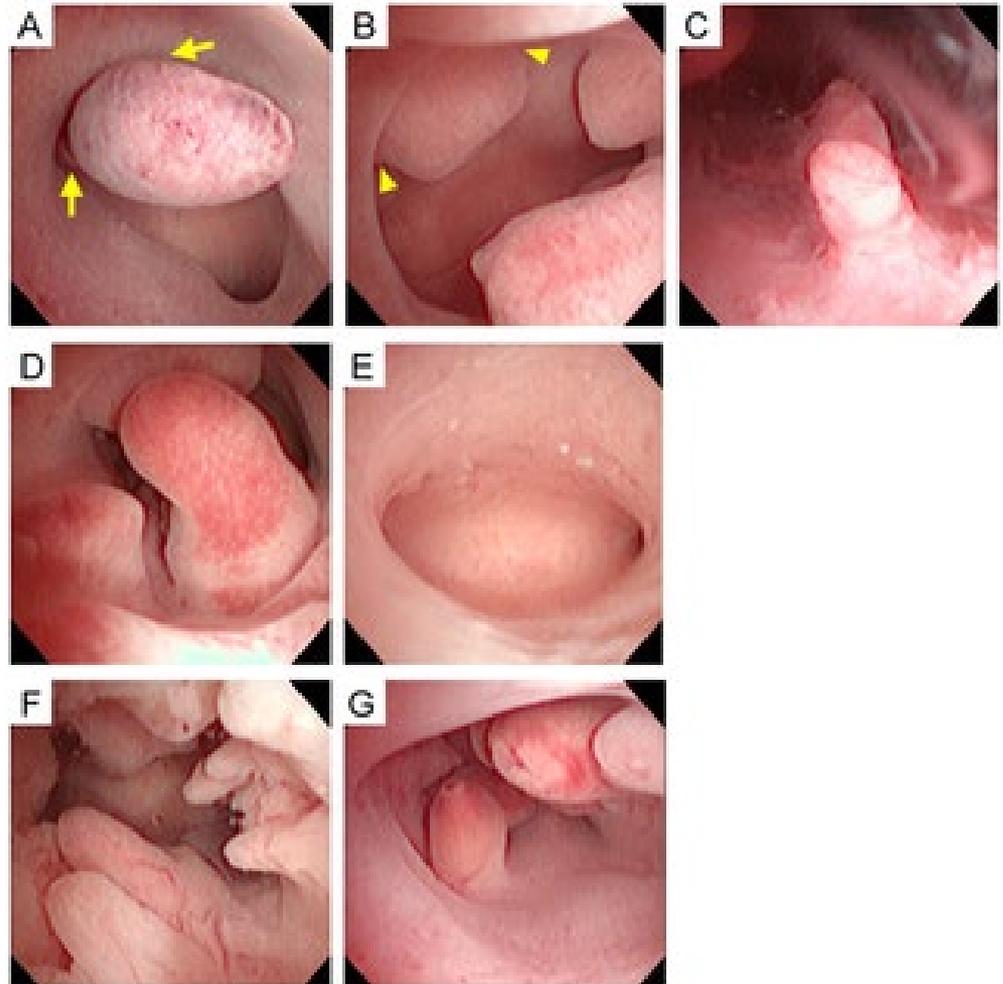
- **Address male factor**

- Referral to Urology
- Lifestyle changes: no smoking!
- Avoid activities that will increase testicular temperature: Boxers not briefs, no hot tubs
- Treat hormonal problems: Clomiphene, hCG injections, Pergonal
 - 3 – 4 months before you see changes to semen parameters
- Treat physical problems: Varicocele repair, microsurgery to repair damaged vas deferens, retrieve sperm from epididymis or testicle for use in IVF

In general even if hormonal and/or physical problems are treated, IUI or IVF is still usually needed to overcome male factor infertility.

Treatment Of Infertility

- Address Male factor
- **Surgery for female partner if needed**
 - Laparoscopy (fallopian tubes, endometriosis, fibroids)
 - Laparotomy (fibroids)
 - Hysteroscopy (uterine abnormality)



Treatment Of Infertility: Ovulation Induction

- Address male factor
- Surgery for female partner if needed
- **Ovulation induction with or without IUI**
 - Clomiphene citrate / Letrozole
 - 8 - 10% chance of success per cycle
 - Injectable Gonadotropins (FSH or FSH/LH combos)
 - 15 - 20% chance of success per cycle



****Always perform ultrasound prior to ovulation to confirm number of follicles that could release****

Treatment of Infertility: Intrauterine Insemination

- Bypasses the cervix and places sperm directly into the uterus
- Most successful when total motile sperm is greater than 10 million
- IUI is most successful in:
 - Female infertility due to ovulatory dysfunction/timing, cervical mucus factor, or cervical scarring
 - Male infertility
 - Donor sperm insemination



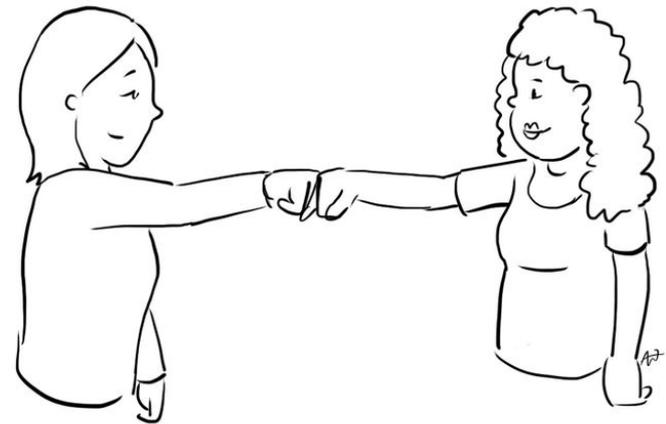
Treatment Of Infertility

“If every test is normal, why can’t we get pregnant?”

• Unexplained Infertility

- Incidence 25%
- Treatment
 - Wait and see
 - Ovulation induction + IUI
 - 3 – 6 cycles only
 - In Vitro Fertilization (IVF)
- Potential causes:
 - Fertilization abnormalities
 - Embryonic development
 - Implantation

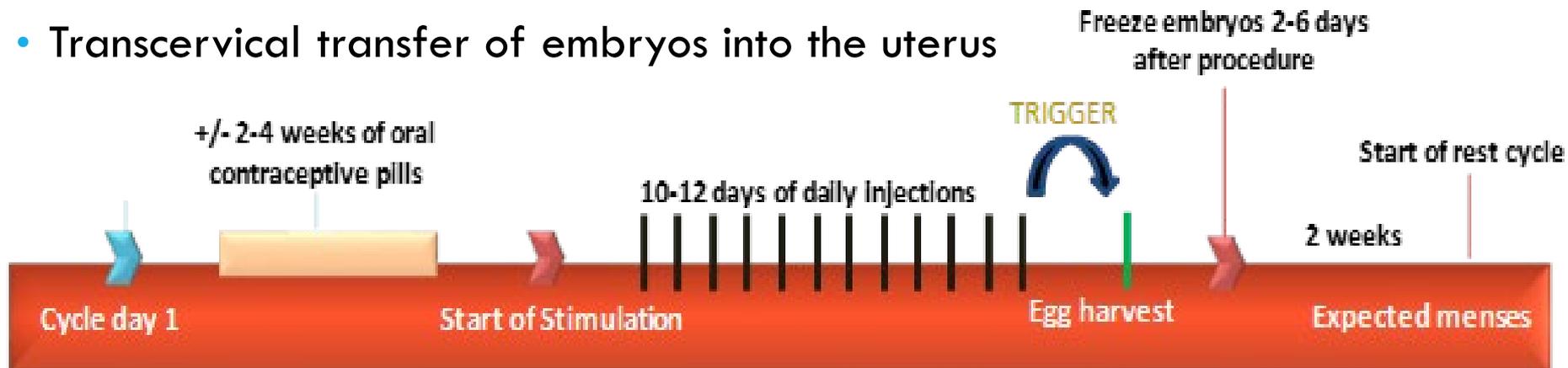
For those going through the same thing, nothing needs to be said.
We get it sucks.



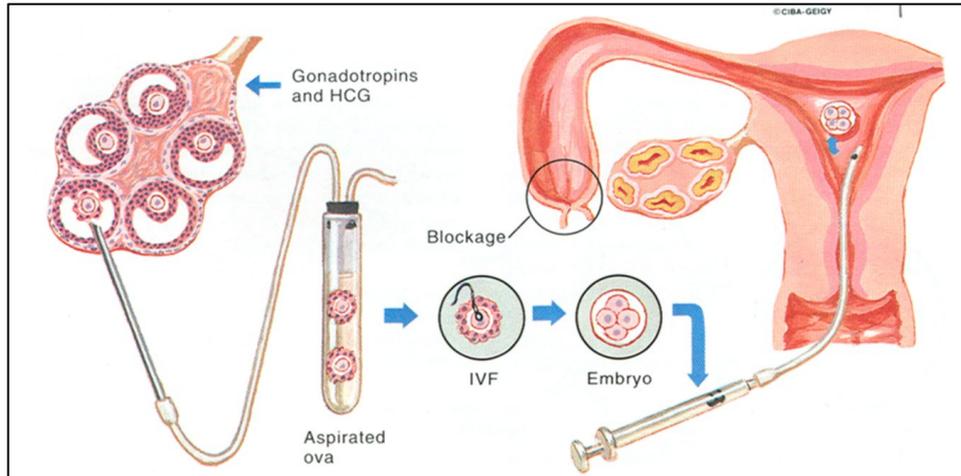
But you just have to believe...
Not if, but when.

In Vitro Fertilization (IVF)

- Sequence of highly coordinated steps beginning with controlled ovarian hyperstimulation with injectable gonadotropins for ~10 days
- The retrieval of oocytes is timed using a special injection called a trigger and the oocytes are removed from the ovaries under transvaginal ultrasound guidance (no incisions!)
- Fertilization happens in the laboratory and embryos are frozen for future transfer.
 - Chromosomally screening (PGT) can be performed on embryos.
- Transcervical transfer of embryos into the uterus



In Vitro Fertilization



- Fallopian Tube disease
- Endometriosis
- Severe Male Factor Infertility
- Multifactor or Unexplained Infertility
- Advanced Reproductive Age
- Premature Ovarian Failure
- Mullerian anomalies
- Medical Disease
- Genetic Disorders
- Previous treatment failures
- Fertility preservation



Patient Resources

- American Society for Reproductive Medicine (ASRM)
 - www.asrm.org
- Resolve – National Infertility Support Group
 - <https://resolve.org/>
- Society for Assisted Reproductive Technology
 - www.sart.org
- Polycystic Ovarian Syndrome
 - <https://www.pcosaa.org/>
- Endometriosis
 - <http://www.endometriosisassn.org/>
- CDC - Assisted Reproduction Technology
 - <http://www.cdc.gov/ART/index.htm>
- FertilityIQ
 - www.fertilityiq.com





Questions?

Thank you !

Email: jessicaboonepa@gmail.com