Fertility Evaluation for the Generalist

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DISCLOSURES: None

LEARNING OBJECTIVES: At the conclusion of this presentation, participants should be able to:

1. Define Infertility and identify those who need evaluation
2. Perform an evidence-based infertility workup
3. Recognize common female and male causes of infertility
4. Initiate appropriate first-line treatment
5. Identify indications for referral to REI specialists

Why Infertility Matters

1. Infertility affects 10-15% of couples

2. Increasing maternal age is a major contributor

3. Significant emotional, financial, and psychosocial burdens

4. General Ob-Gyns are often the first point of contact

ASRM Definition of Infertility Oct. 2023

Infertility is a disease, condition, or status characterized by any of the following:

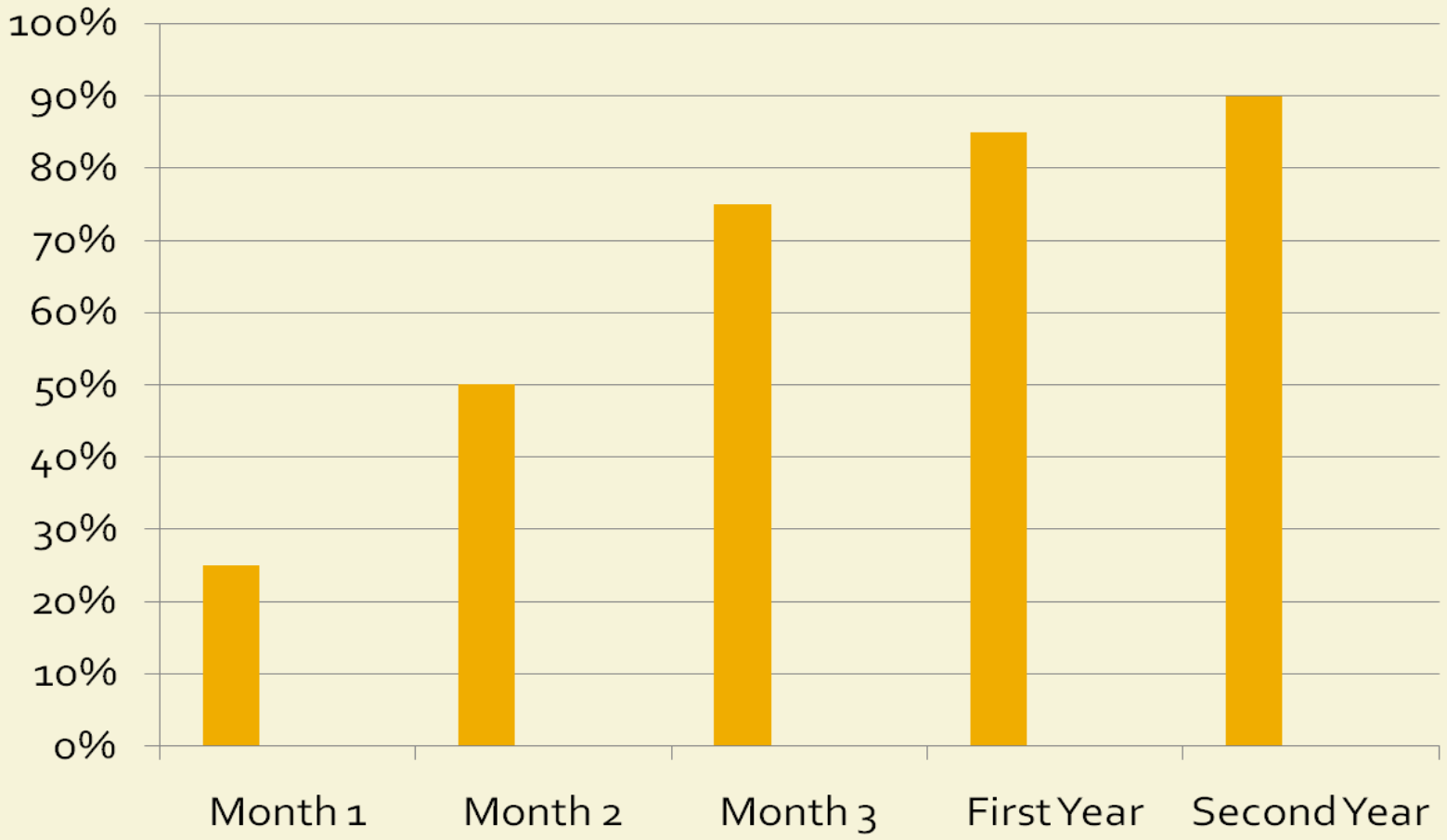
- The inability to achieve a successful pregnancy based on a patient's medical, sexual, and reproductive history, age, physical findings, diagnostic testing, or any combination of those factors. (New 2023)

- The need for medical intervention, including, but not limited to, the use of donor gametes or donor embryos in order to achieve a successful pregnancy either as an individual or with a partner. (New 2023)

- In patients having regular, unprotected intercourse and without any known etiology for either partner suggestive of impaired reproductive ability, evaluation should be initiated at 12 months when the female partner is under 35 years of age and at 6 months when the female partner is 35 years of age or older.

Normal Pregnancy Rates in Newly Married Couples

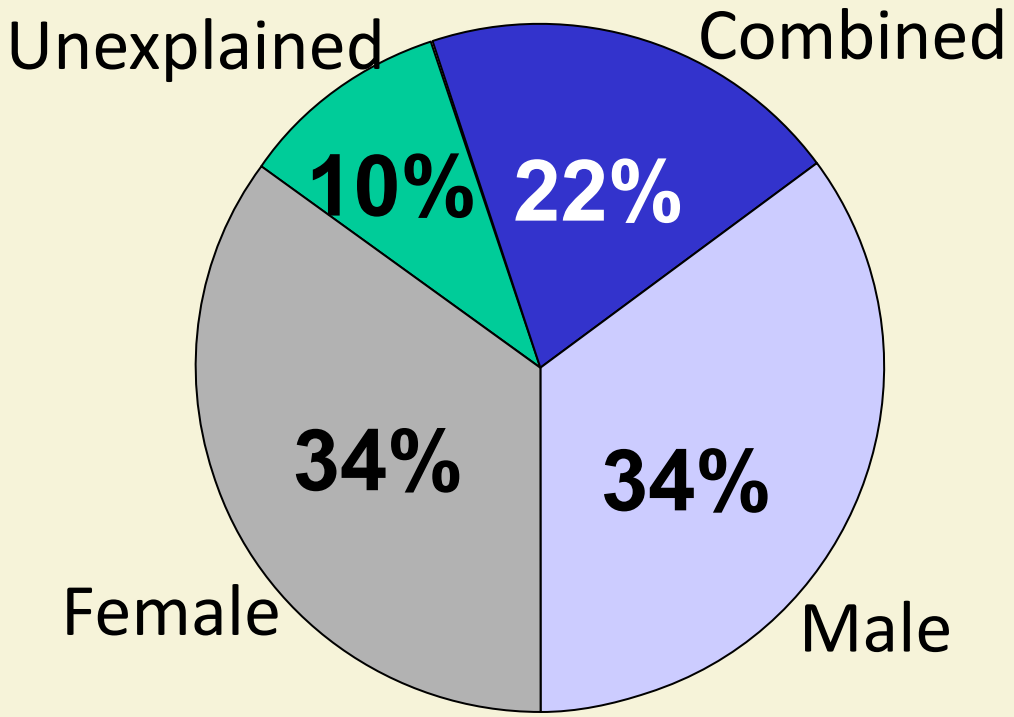
(85% are pregnant after the first year, 90% are pregnant after two years)



http://www.uptodate.com/contents/overview-of-infertility

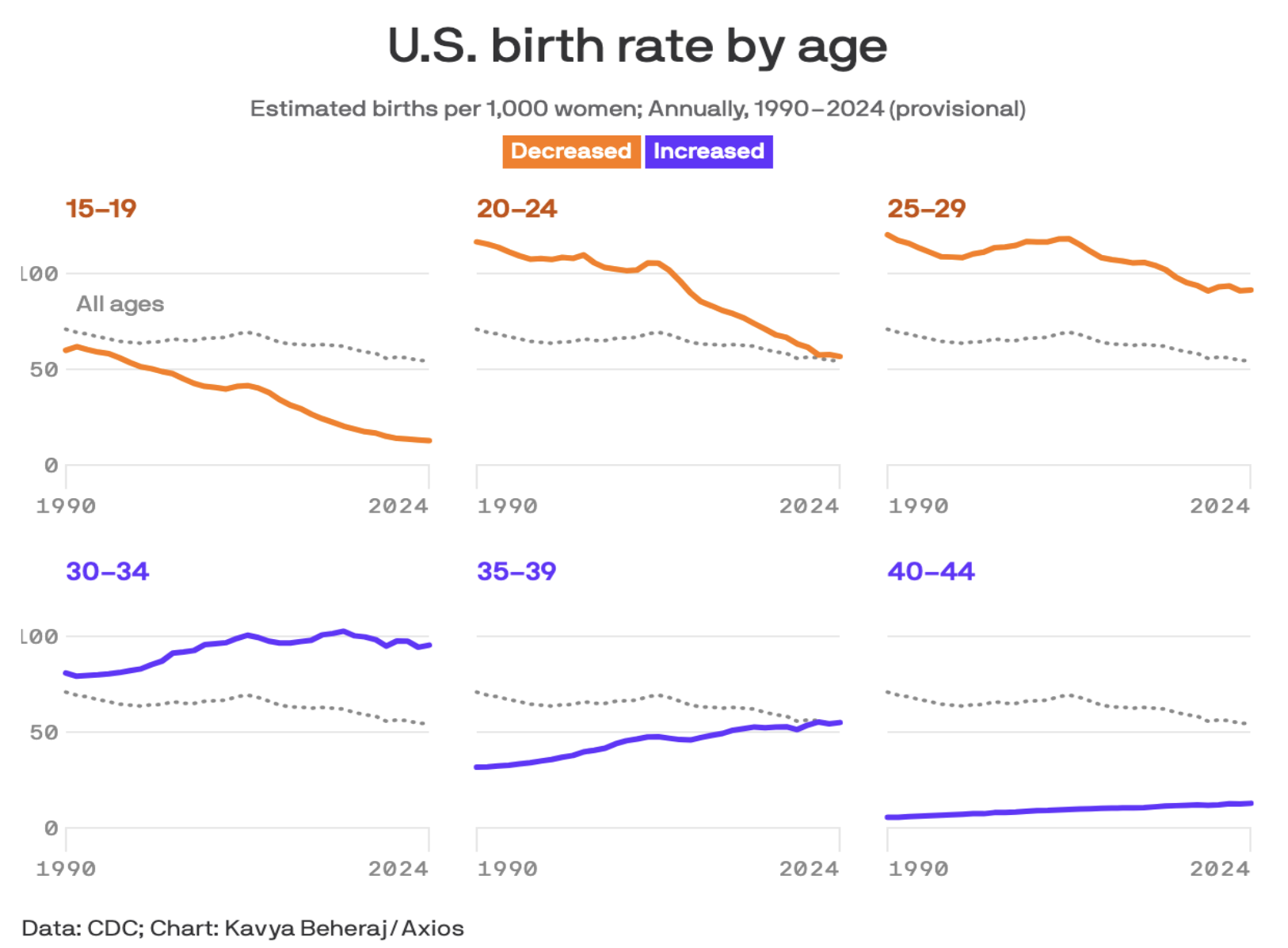
Causes of Infertility

- Male Factors (1/3)
  - Poorly functioning and/or few sperm
- Female Factors (1/3)
  - Ovulatory problems
  - Tubal Problems
  - Uterine Problems
  - “Hostile” Peritoneal Environment
- Combined or Unknown Factors (1/3)



ASRM. Fertility evaluation of infertile women. Fertil Steril 116: 1255-1265,2021

US Birthrate of 1.6 Falls Below Replacement of 2.2



Women in their 20's are delaying childbirth until their mid to late 30's

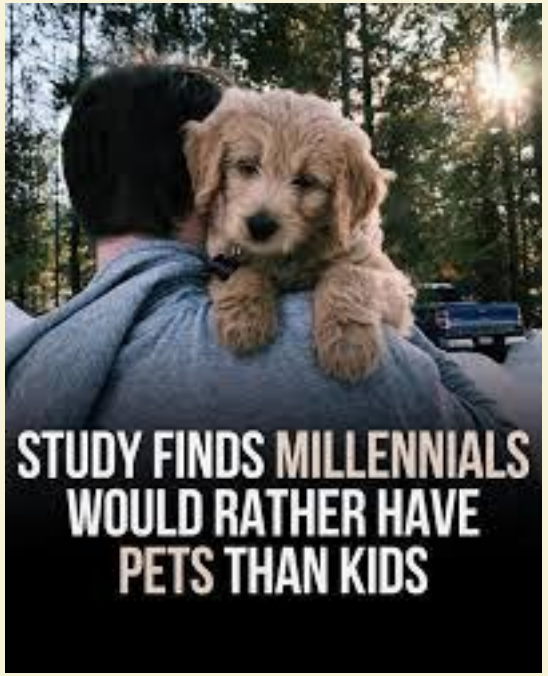
Women in their 30's and early 40's are increasing their birth numbers, often with assisted reproduction

134 million Households in the US –March 2026

71 million (53%) have a Dog

59 million (44%) have a Cat

54 million (40%) have a Child < 18 years

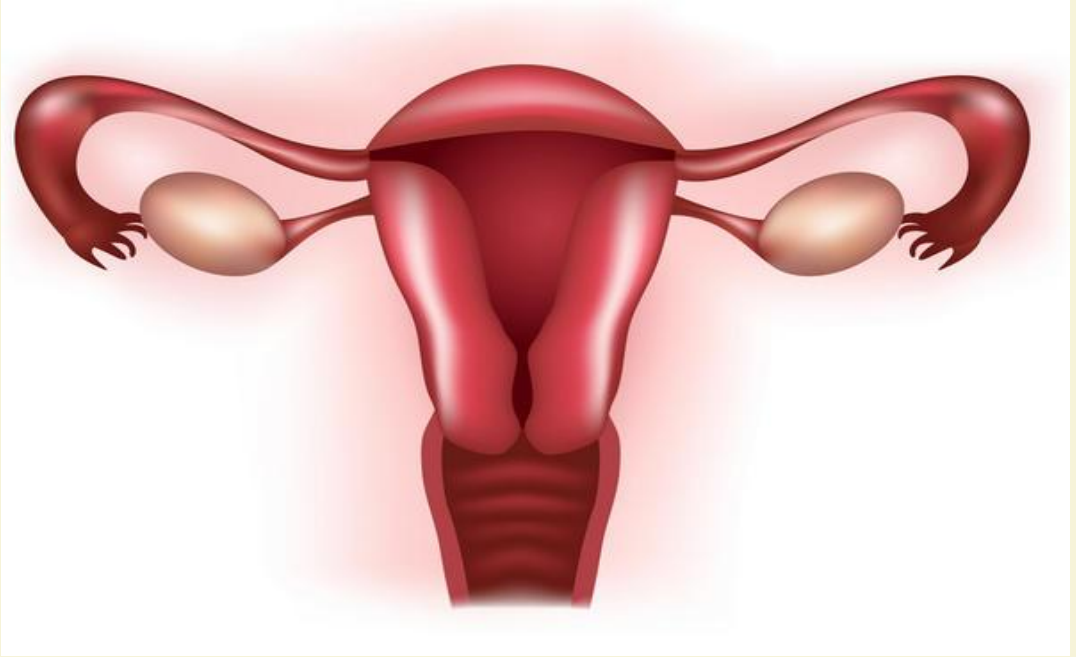


US Households (monthly) – Y Charts from the US Census Bureau. March 2026.

Consumer Affairs Research Team. Millennials prefer pets to children. Survey. Journal of Consumer Research. June 12, 2024.

Requirements to achieve Natural Heterosexual pregnancy

1. Are the tubes patent?
2. Are sperm adequate?
3. Is the uterus normal?
4. Is ovulation occurring?
5. Adequate intercourse?



Most infertility cases can be diagnosed after answering these questions.

When to Initiate the Evaluation of Infertility Patients

Unprotected intercourse, no contraception, and without conception

AGE OF FEMALE	WHEN TO START EVALUATION
< 35 years	After one year of trying
35 to < 40 years	After 6 months of trying
40 or more years	Immediately

Most people diagnosed with infertility are in reality “Sub-fertile”

Primary Management of Infertility

- Identify risk factors

  (Age, menstrual history, STD, prior surgery, tobacco, alcohol, obesity, radiation, toxins, sexual function, prior pregnancies)

- Perform essential investigations

  (HSG, semen analysis, documented ovulation)

- Counsel couple

  (age, years of trying, prior treatments)

- Initiate treatment or refer

ASRM Practice Committee. Fertil Steril 116:1255-1265 , 2021.

Causes of Female Infertility: Ovulation Disorders

Ovulatory Dysfunction

-Polyendocrine Metabolic Syndrome (PCOS)

-Hyperprolactinemia

-Hypothyroidism

-Idiopathic Hypothalamic hypogonadism(IHH)

-Premature ovarian failure (POF)

Decreased Ovarian Reserve

-Advanced age of the female

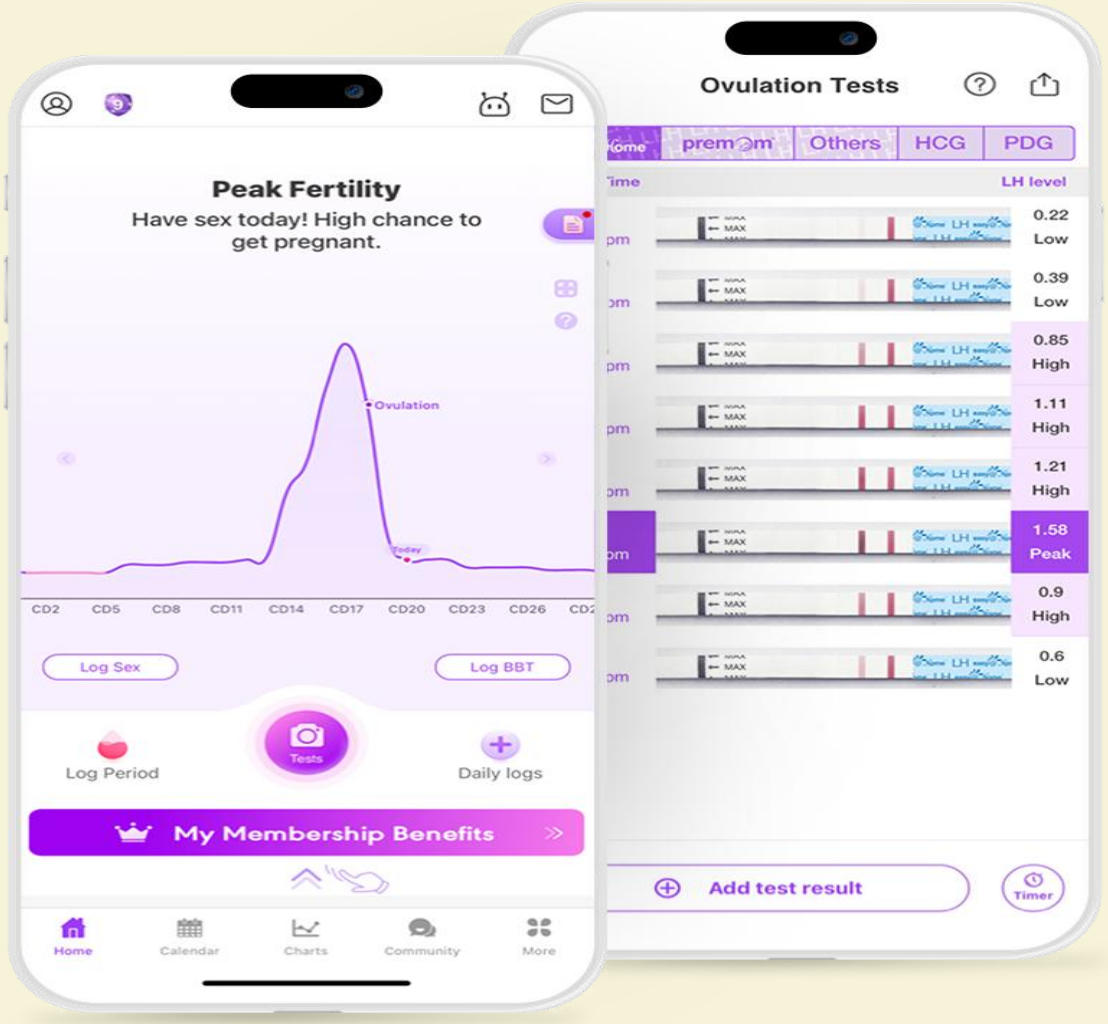
- Prior chemo and/or radiation therapy
- Prior surgery on the ovary
- Turner mosaic, Fragile X premutation
- Smith-Lemli-Opitz syndrome
- FSH > 10 miu/ml, AMH < 1 ng/ml

-Antral (2-9 mm)follicles < 8

ACOG. Infertility work up for the women's health specialist. 2019
ASRM. Fertility evaluation of infertile women. Fertil Steril 116: 1255-1265,2021

Tests to aid in the Evaluation of Ovulatory Disorders

- Normal Ovulatory Function
  - --Normal menstrual cycle (26-34 days)
  - --Positive urinary LH surge at midcycle
  - – Cycle day 21 Progesterone: > 10 ng/ml
  - – Midcycle ultrasound of follicles
  - – TSH: 1.0 to 4.1 mIU/ml
  - – Prolactin: < 25 ng/ml
  - – HgbA1c: < 5.7%



ASRM. Fertility evaluation of infertile women. Fertil Steril 116: 1255-1265,2021

Premom – 25 strips for $10 on Amazon

Ovarian Reserve Testing

- May disrupt Normal Ovulatory Function

  (if levels are outside the range)

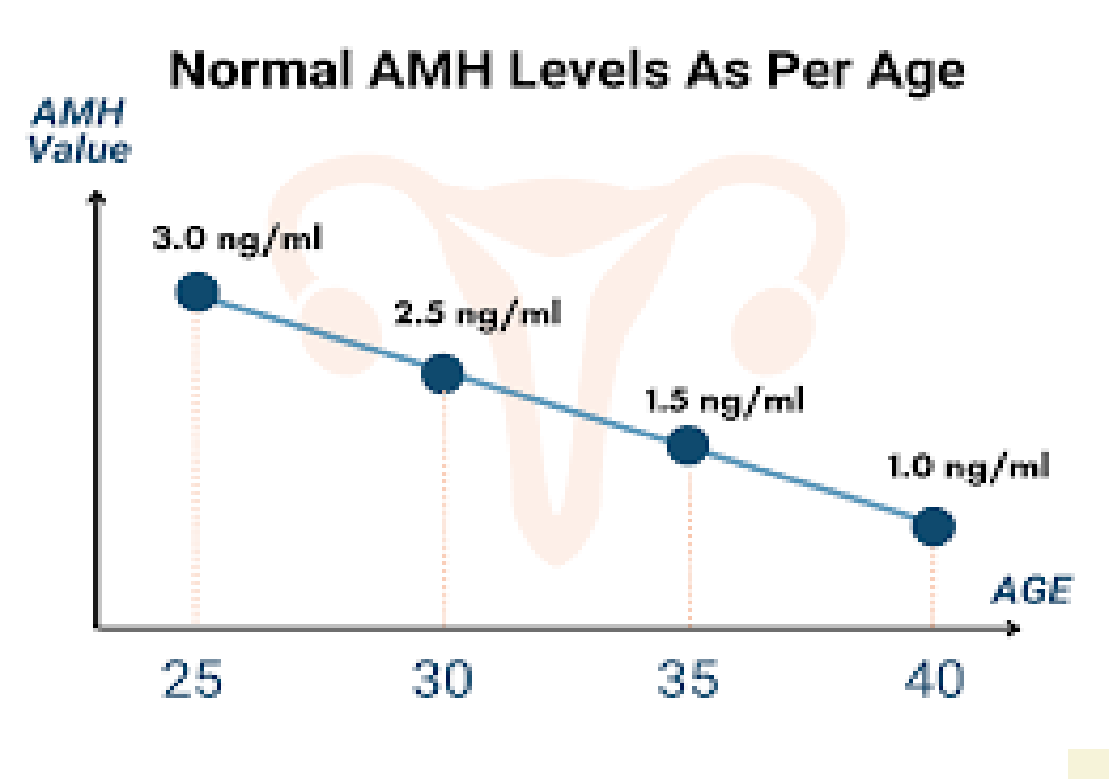
  – Cycle Day 3 FSH: <10 mIU/L

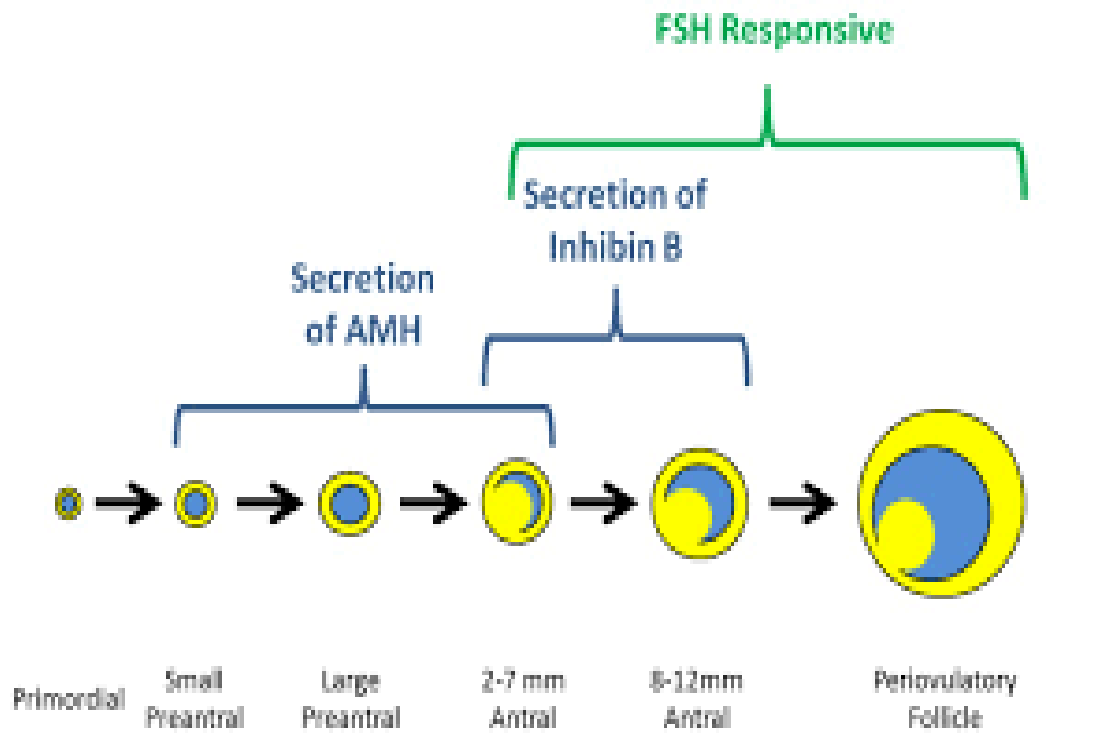
  – Cycle Day 3 Estradiol: < 60 pg/ml

  – Any cycle day AMH: 1.5 to 4.0 ng/ml

ASRM. Fertility evaluation of infertile women. Fertil Steril 116: 1255-1265,2021

Anti Mullerian Hormone (AMH) Correlates with Ovarian Reserve





Decreased AMH associated with increased age, obesity, tobacco use, endometriosis, genetic factors, chemotherapy, radiation therapy

AMH is produced by the small preantral and antral Follicles (2-9mm) and correlates to the ovarian reserve

ASRM Committee Opinion: Measures of Ovarian Reserve. Fertil Steril 114:1151-1157, 2020.

Interpretation of Female Day 3 Hormonal Profile

FSH	LH	Estradiol	AMH	Testosterone	Diagnosis
3-10 miu/ml	2-10 miu/ml	<60 pg/ml	1-4 ng/ml	10-70 ng/dl	**Normal range**
3	6	45	3.0	30	**normal**
18	6	Normal or high	>5.0	Normal or elevated	**PCOS**
Often >10, Low if E2 Hi	>10	Normal or high	<1.0	normal or low	**Ovarian hypofunction**
>40	elevated	Often <50	Very low	low	**Ovarian failure**

Premature Ovarian Insufficiency: Evidence-based guideline. Fertil Steril. 123: 221-236, 2025.

Polyendocrine Metabolic Ovarian Syndrome (PMOS)

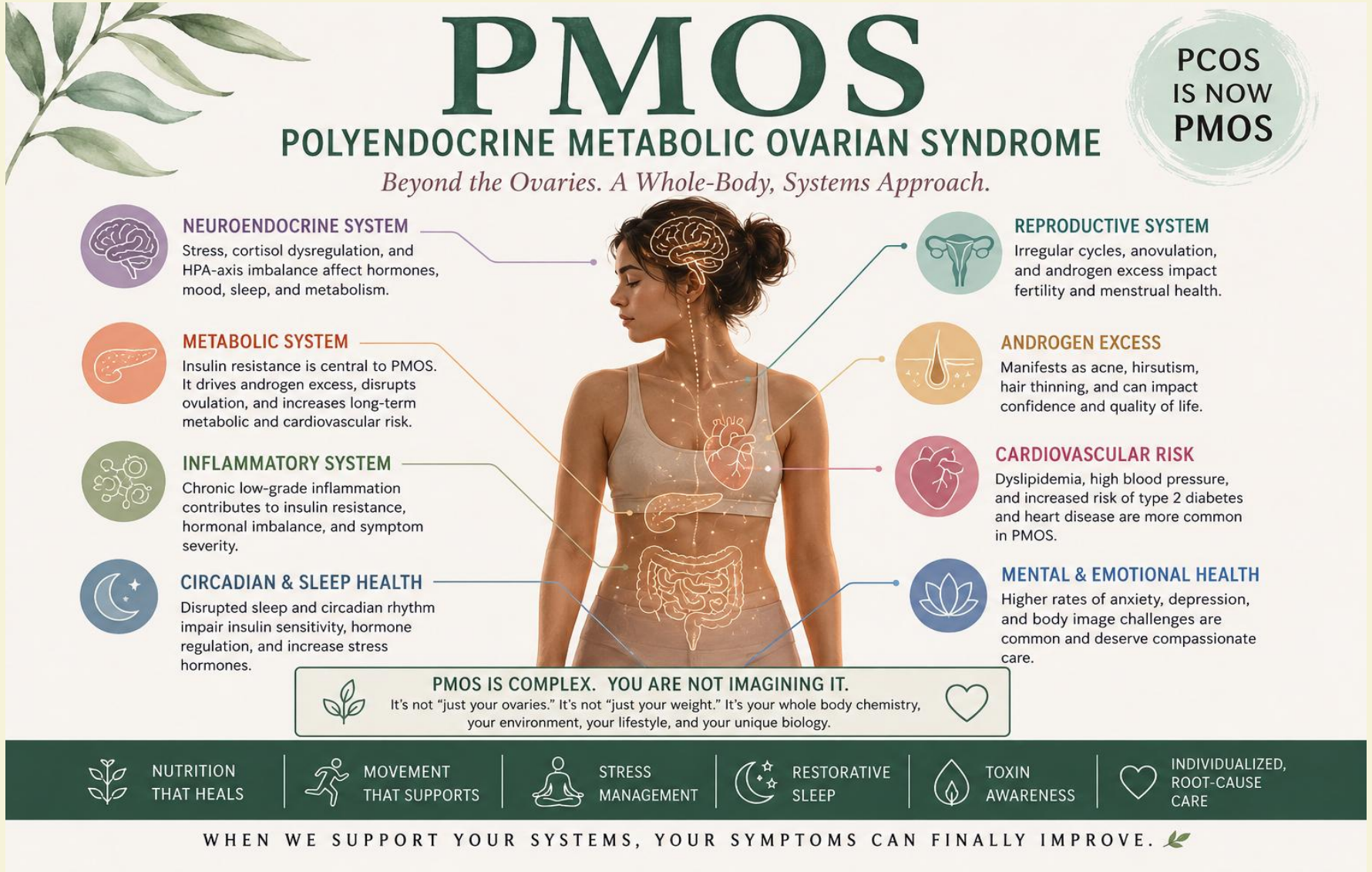
- New name for polycystic ovary syndrome (PCOS)
- Old term implied pathologic ovarian cysts
- Obscured diverse endocrine and metabolic features
- Affects 1 in 8 women or 170 million globally
- Includes oligo-ovulation, clinical or biochemical hyperandrogenism, and polycystic ovaries on ultrasound or elevated AMH (>7.8) New 2026
- Adolescents age 10-19 require the first two

Teede HJ and the Global Name Change Consortium. The Lancet. May 12, 2026. DOI: 10.1016/S0140-6736(26)00717-8

Ou M et al. AMH is a good predictor of Metabolic Risk in women with PCOS. Int J Endocrinol. 2021 Aug 12;2021:9511772. doi: 10.1155/2021/9511772

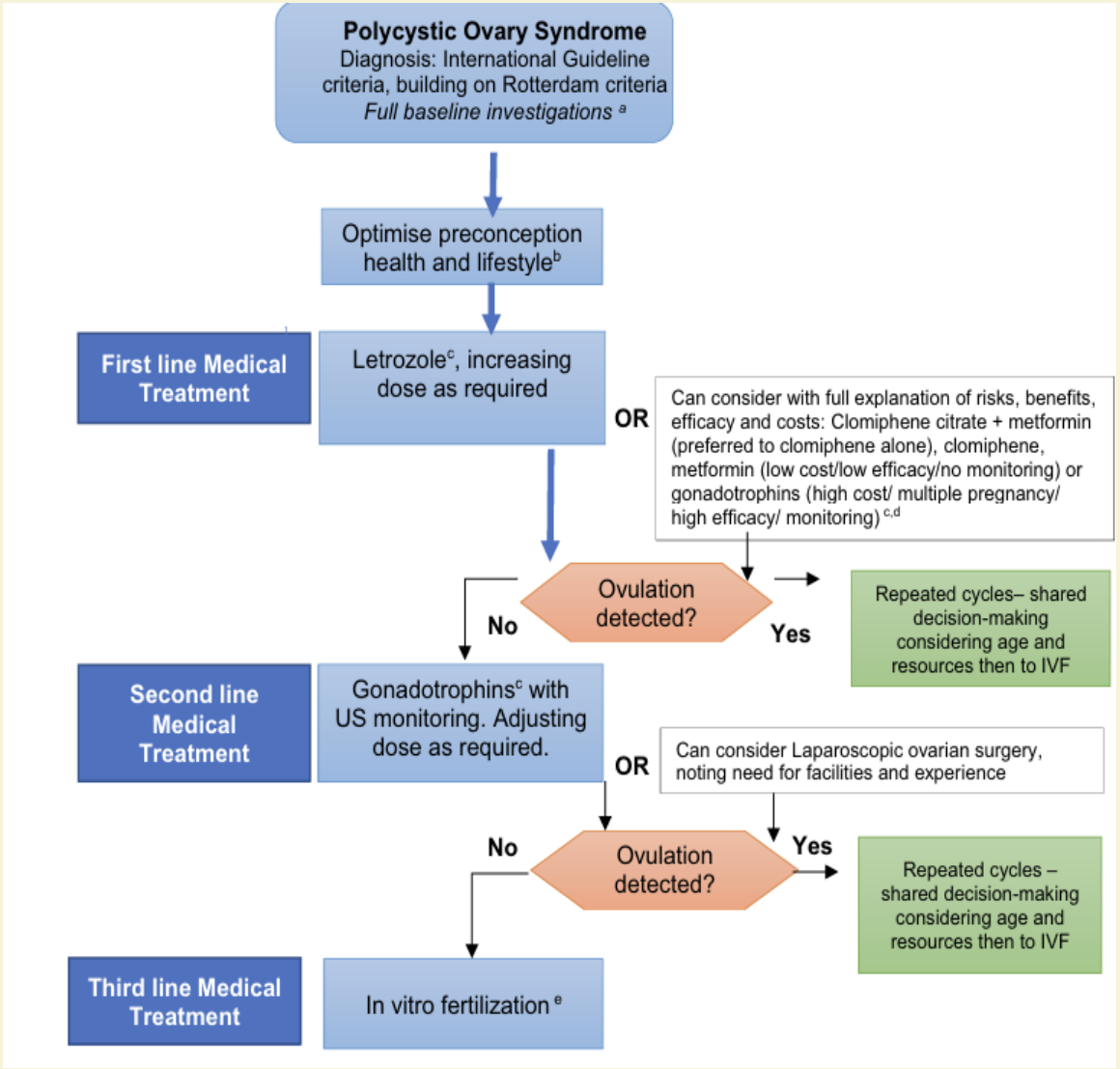
New 2026

Beyond the Ovaries: A Whole-Body Systems Approach



Treatment of PMOS

International Guideline for Management of PCOS. Fertil Steril 120:767-793, 2023.



Fertility Treatments to Induce Ovulation

- Clomiphene 50 mg cycle days 3 to 7 ($30.00/5)
- PMOS: Letrozole of 2.5 mg cycle days 3 to 7 ($2.00/5)
- For PMOS patients (with elevated HgbA1c)

  -Metformin ER 500 to 750 mg po daily to BID ($28.00/180)
- Vaginal progesterone supplements 3 days after LH surge
  - Vaginal suppository compounded 100 mg ($2.50/each)
  - Endometrin Micronized vaginal tablet 100 mg ($15/tablet)
  - Crinone 8% vaginal gel daily ($40/applicator)
  - Prometrium capsule 100 mg used vaginally-off label ($3.50/each)

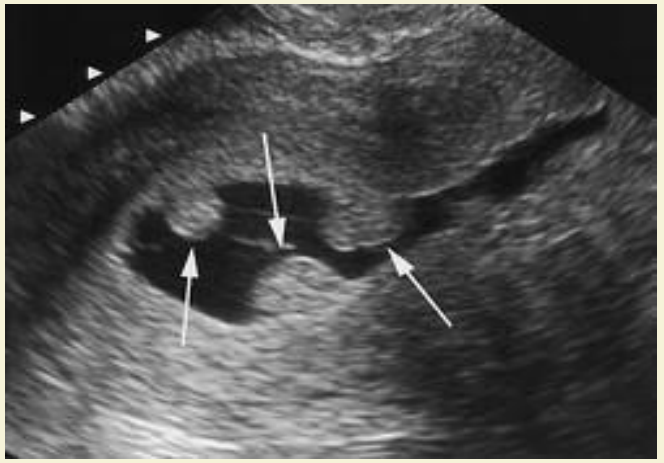
Rule of 7's for Ovulation Induction

Treatment Cycle	Rule	Days
• Use Clomiphene 50 mg cycle days 3 to 7 or Use Letrozole of 2.5 mg cycle days 3 to 7	7	3-7
• Expect ovulation in 7 days after last pill	14	10-18
• Monitor CD 21 Progesterone in 7 days	21	19-23
• Check pregnancy test 7 days later	28	28-30

Causes of Female Infertility: Uterus and Tubes

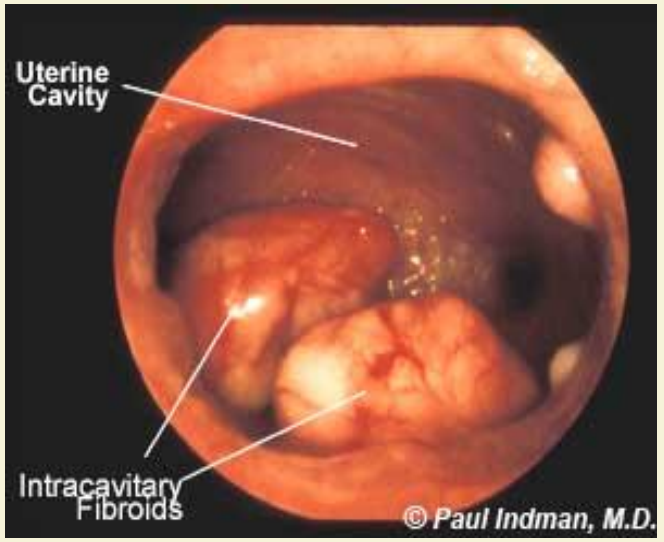
Uterine Factors

- Fibroids
- Polyps
- Asherman's syndrome scarring
- Endometriosis/Adenomyosis
- Congenital anomalies

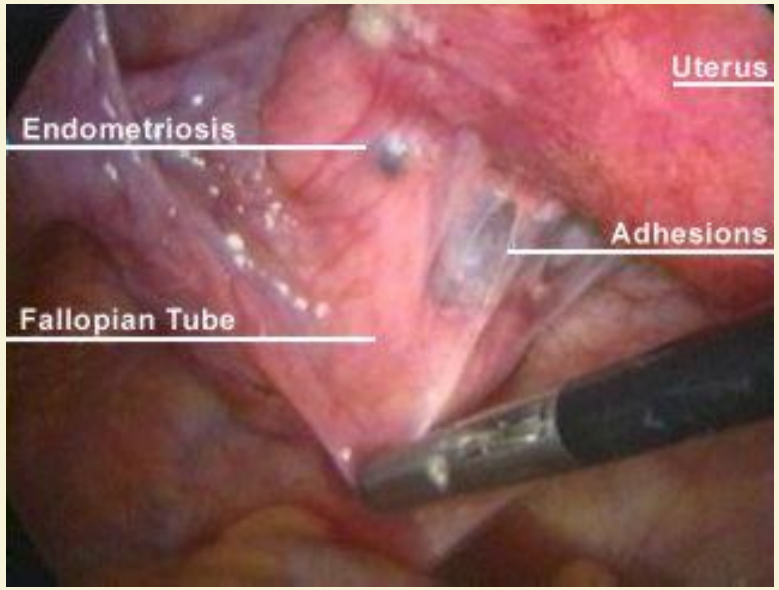


Tubal Factors

- Hydrosalpinges
- Blocked or damaged tubes
- Prior infection
- Prior surgery



Fertility treatments: Anatomic Abnormalities



– **Diagnosis**

HSG

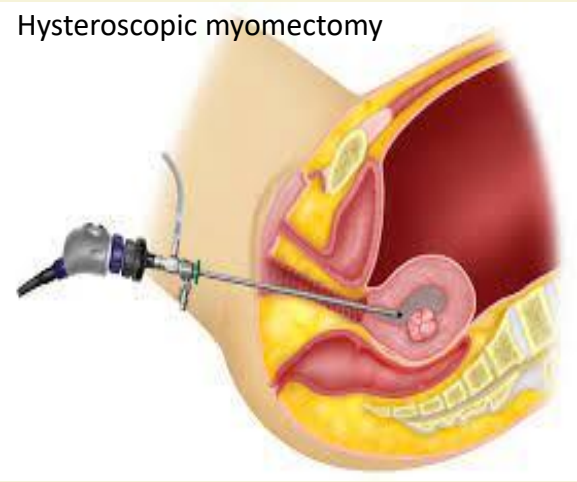
Laparoscopy

SHG

– **Surgical intervention**

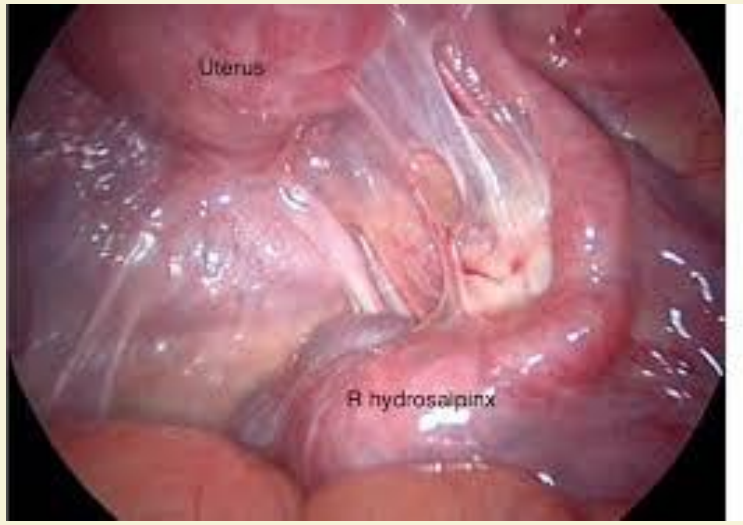
- Hysteroscopy
- Laparoscopy
- Open abdominal surgery

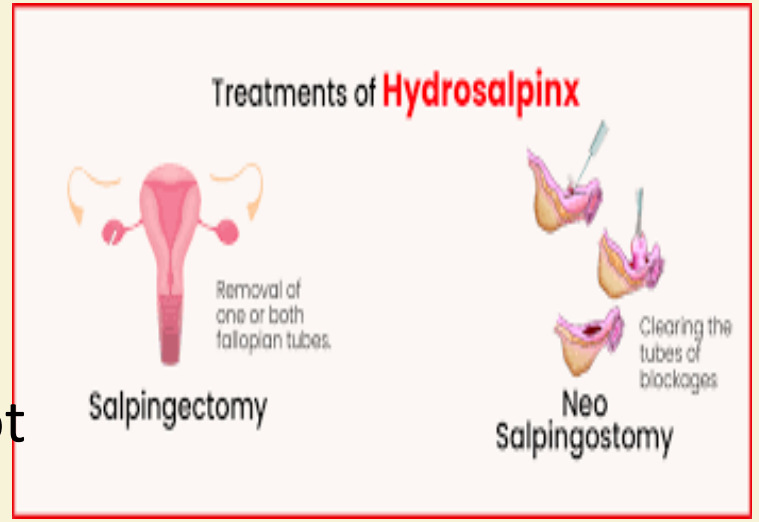
Hysteroscopic myomectomy



Hydrosalpinx Treatment Options

- Antibiotics -if Pelvic Inflammatory Disease
- Salpingectomy (tubal removal)-usually best
- Salpingostomy (tubal repair)-ectopic risk
- In vitro fertilization- after tubal removal or occlusion
  -reduces negative impact of tubal fluid
  -reduces embryotoxic cytokines
  -reduces fluid drainage through uterus
  -enhances embryo implantation
- Note: Proximal occlusion without hydrosalpinx does not require surgical intervention





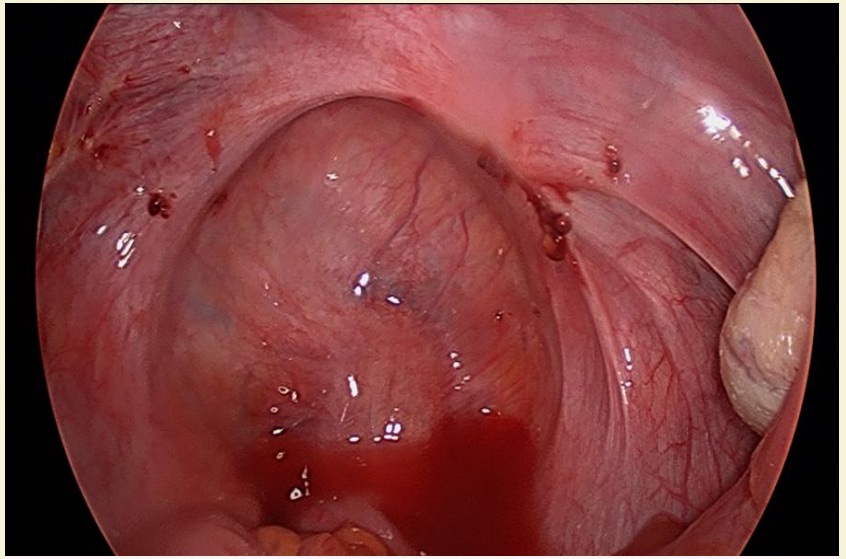
Endometriosis , Adenomyosis, Endometriomas

- Causes: retrograde menses, lymphatic and circulatory spread, embryonic cell growth, immune dysfunction, hormonal imbalances

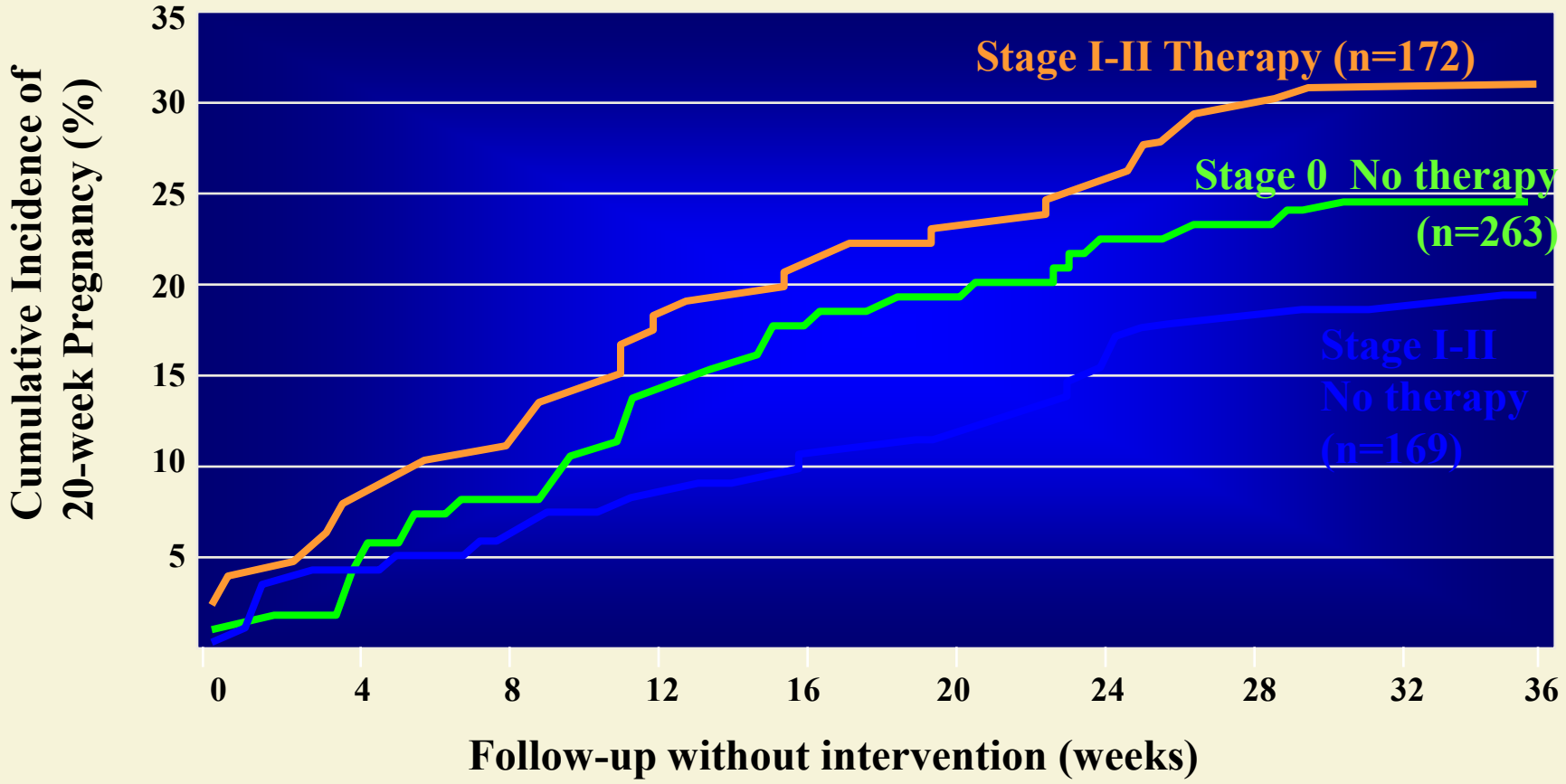
- Symptoms: dysmenorrhea, dyspareunia, chronic pelvic pain, infertility, irregular bleeding

- Effects: inflammation from cytokines, impaired tubal function, reduced fertilization and implantation

- Treatment: Medical [NSAIDs, OCPs, hormonal IUDs (Mirena), progestogens, antagonists (Lupron), agonists (Orlissa); Surgical [laparoscopy, hysterectomy]



Fecundability After Surgical Treatment of Endometriosis



ENDOCAN. Marcoux S. NEJM 1997;337:269

Causes of Male Factor Infertility

OBSTRUCTIVE CAUSES

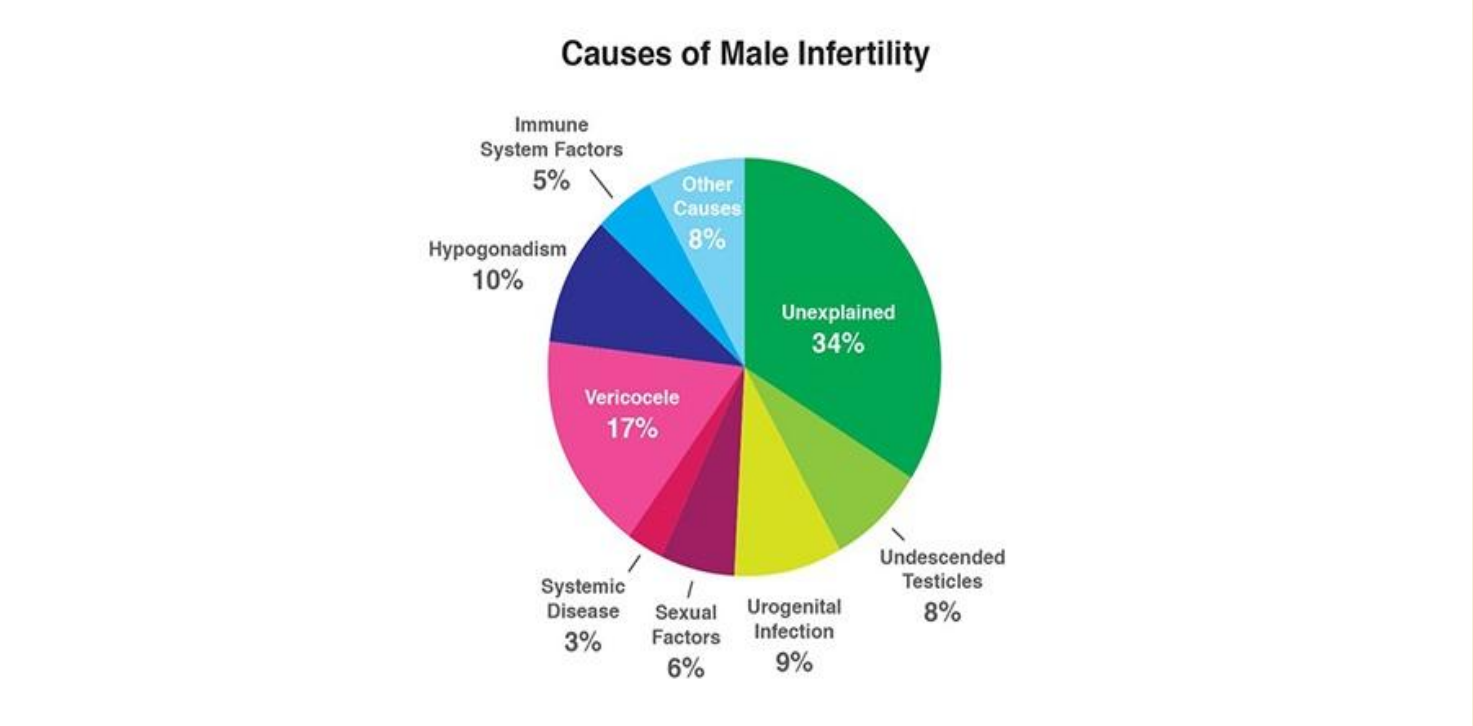
- Azospermia
- Absence of the vas deferens (CFTR)
- Retrograde ejaculation
- Vasectomy

(Check for CF mutation)

NON-OBSTRUCTIVE CAUSES

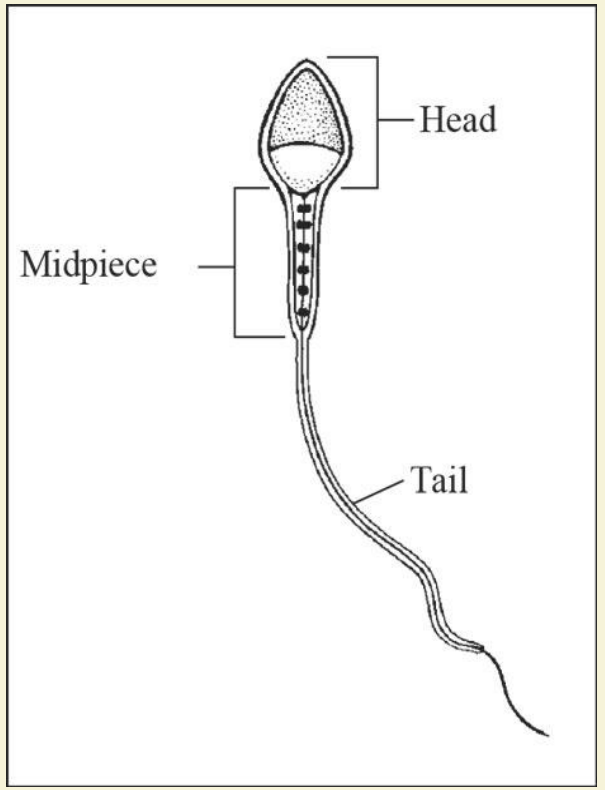
- Testicular insufficiency
- Erectile dysfunction
- Oligospermia (low count)
- Asthenospermia (low motility or abnormal)
- Hypothalamiic

(Check FSH, LH, Testosterone, TSH, Prolactin,
Karyotype, Y-chromosome microdeletion, DNA Fragmentation)



Normal Sperm Parameters

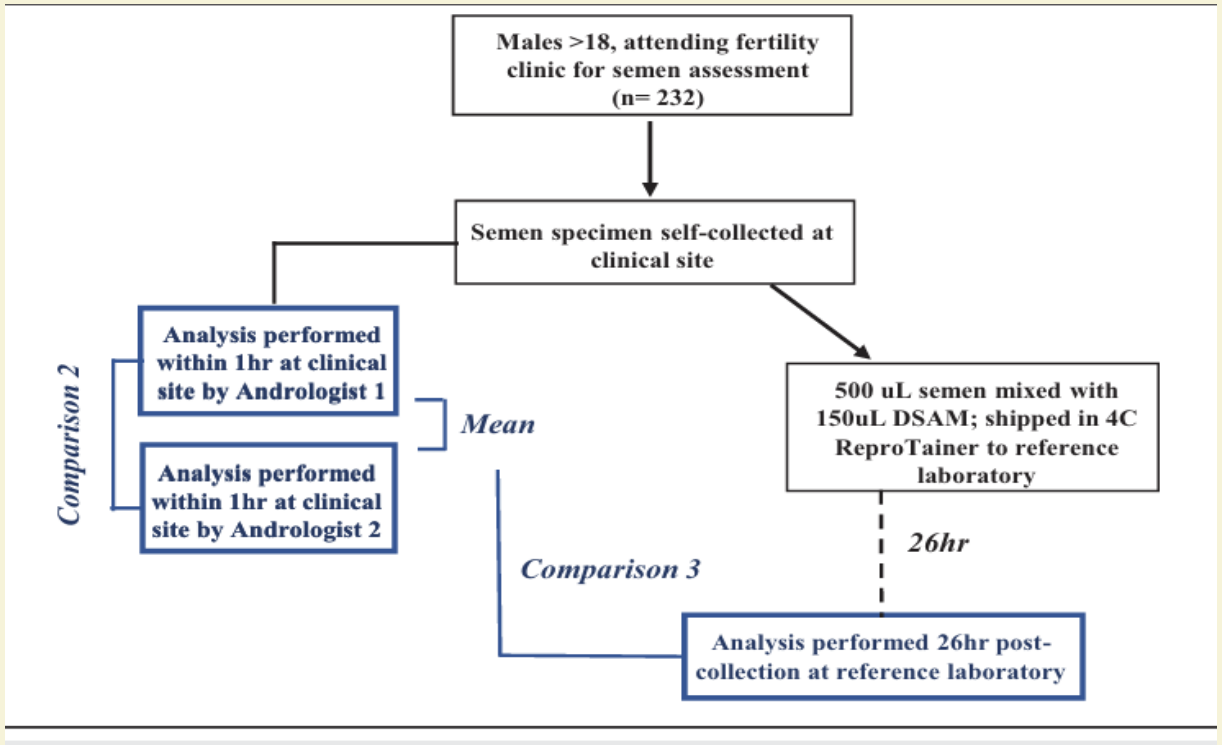
Parameter	Lower reference limit
Semen volume (ml)	1.5 (1.4–1.7)
Total sperm number (10^6 per ejaculate)	39 (33–46)
Sperm concentration (10^6 per ml)	15 (12–16)
Total motility (PR + NP, %)	40 (38–42)
Progressive motility (PR, %)	32 (31–34)
Vitality (live spermatozoa, %)	58 (55–63)
Sperm morphology (normal forms, %)	4 (3.0–4.0)
Other consensus threshold values	
pH	≥7.2
Peroxidase-positive leukocytes (10^6 per ml)	<1.0



WHO 6th Edition 2021

Advanced Home Semen Analysis Test Kit (New 2025)

Comparison of test with 1 hour and at home mailed in collection 26 hours later



SAPYEN Advanced Home Test Kit

Total Motility	87.5% Correlation
Concentration	95.2% Correlation
Morphology (Strict)	82.4% Correlation

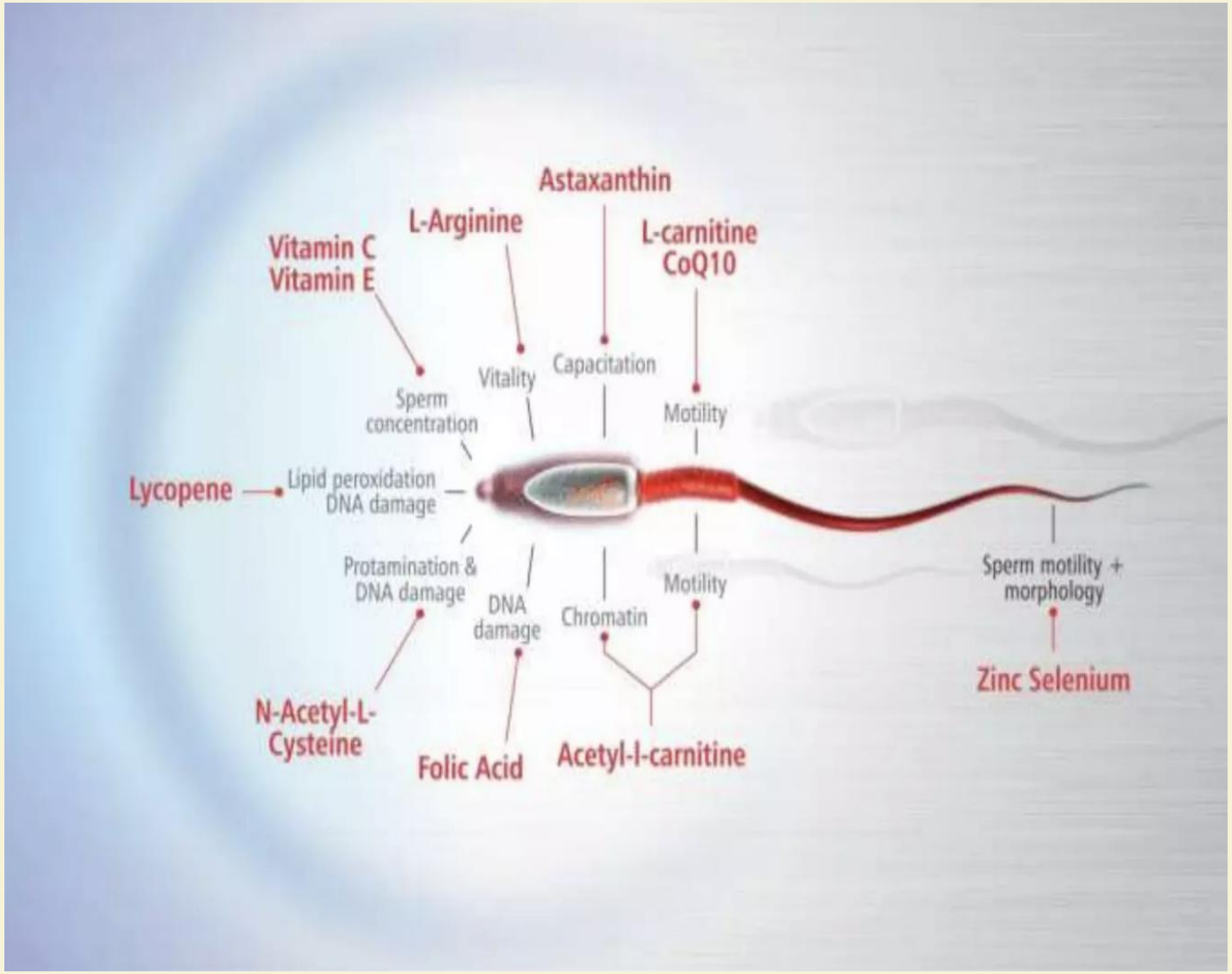
- Stabilization medium (SPX72)
- CLIA-accredited laboratories
- $149 includes shipping and results

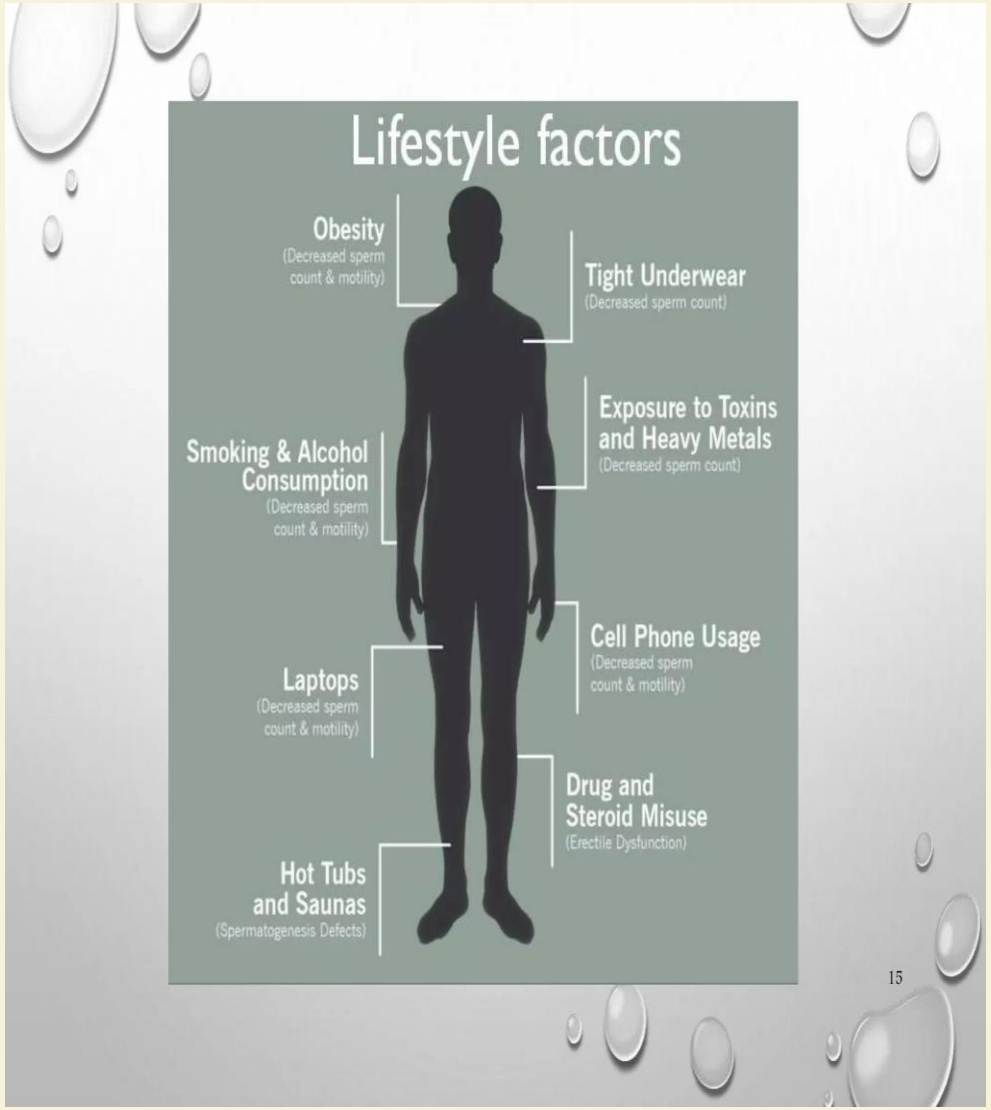
Raccicot K et al. Validation of a mail-in delayed semen analysis protocol developed for home collection. Fertil Steril Reports. 2024;5:378-384.

Interpretation of Male Hormonal Profile

Increased FSH	Increased LH	Low testosterone	Testicular failure
Increased FSH	Normal LH	Normal testosterone	Failure of Spermatogesis
Decreased FSH	Decreased LH	Low testosterone	Hypogonadotropic hypogonadism

Supplements and Lifestyle modification may improve some male factors



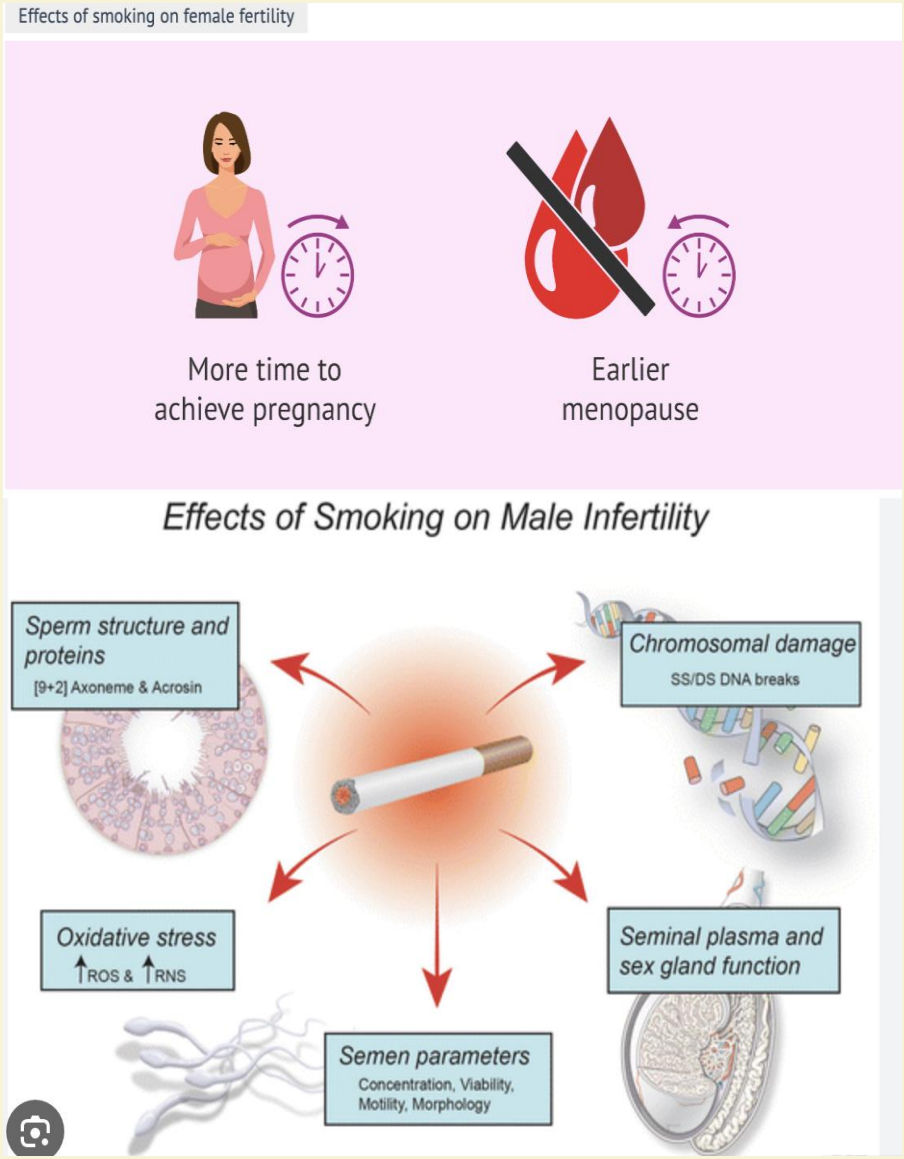


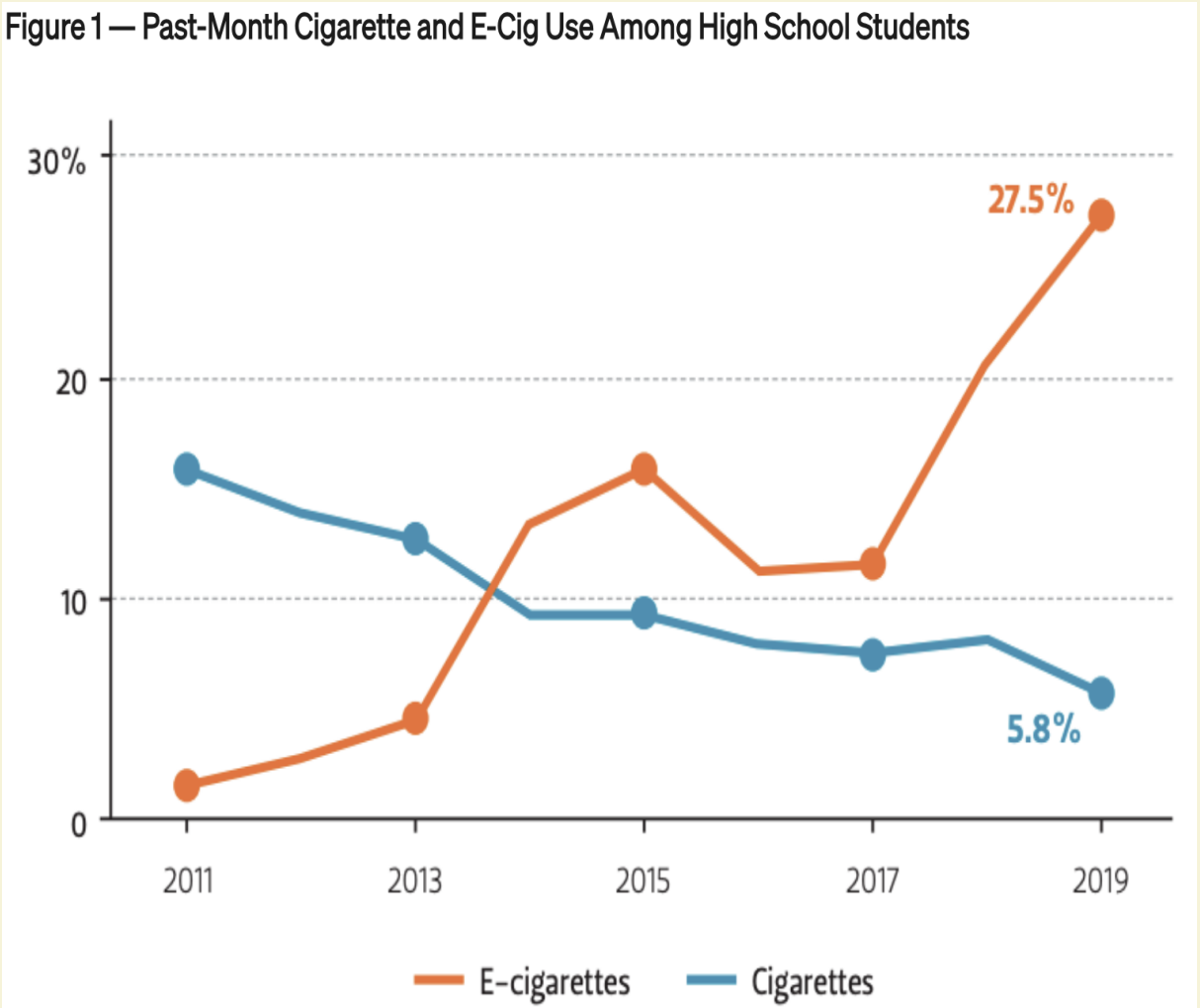
Lifestyle Factors are Modifiable Risks

- Delayed childbearing
- Obesity with BMI > 30
- Smoking
- Excess alcohol
- Poor metabolic health
- Poor nutrition

Emokpae MA and Brown SI. Effect of Lifestyle factors on Fertility. Reprod Fertil. 2021; 2:R13-R26.

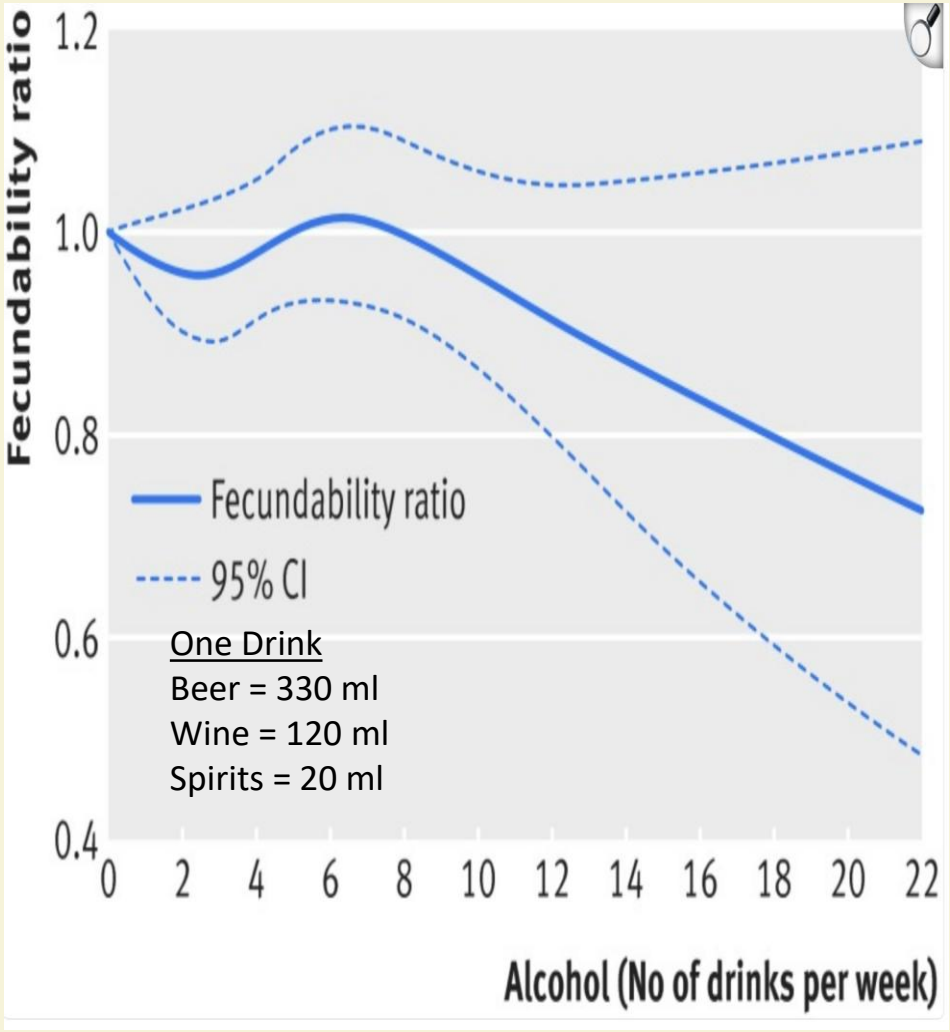
Believe It or Not, 1 Vape has 20- 40 Cigarettes Worth of Nicotine

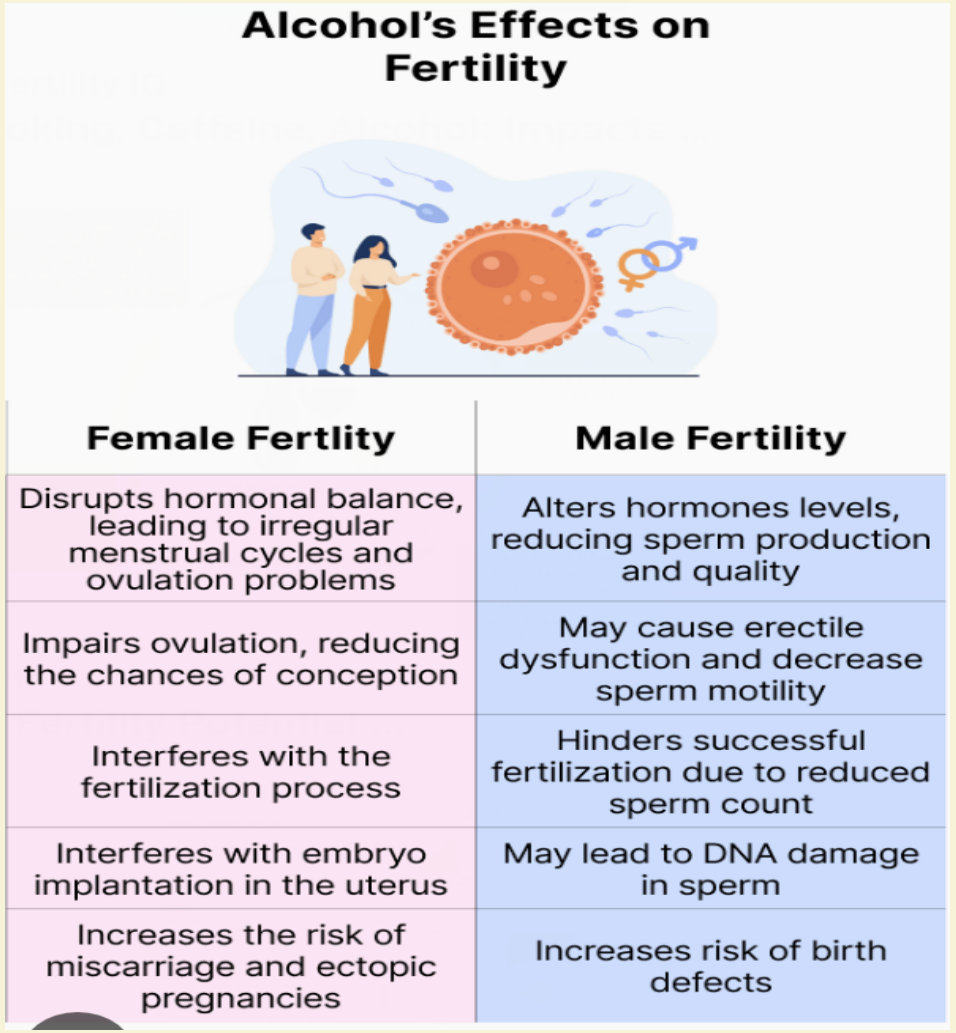




Source *Reuters*, November 5, 2019, https://reut.rs/326yUwJ. Data from National Youth Tobacco Survey, U.S. Food and Drug Administration/Centers for Disease Control and Prevention.

Relation between amounts of pre-pregnancy alcohol consumed per week and fecundability (n=6120)





Mikkelslen EM et al. Brit Med J. 2016 Aug 31, 354::i4262. doi: 10.1136/bmj.i4262

Obesity Negatively Impacts Fertility

MALE FACTOR

Decreased count
Decreased motility
Altered hormones
Erectile dysfunction
Sperm DNA Damage

FEMALE FACTOR

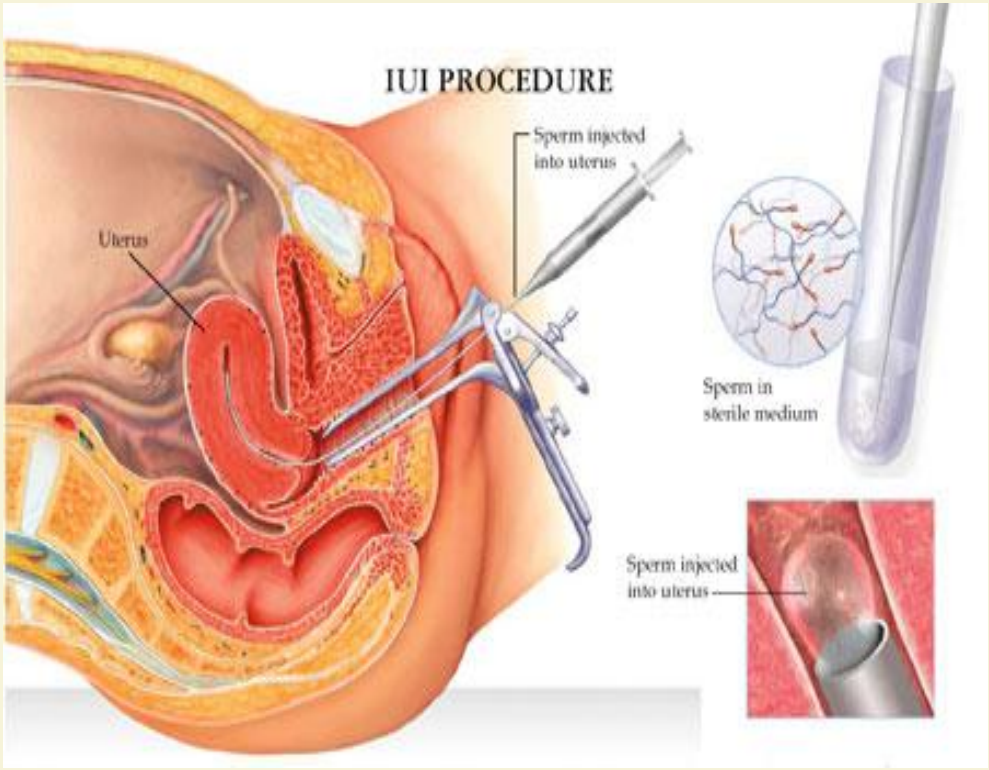
Impaired ovulation
Altered hormones
Disrupted cycles
Reduced egg quality
Increased miscarriage
Lower IVF success
(Down 40% if BMI >40)

OVERALL: Increased time to conceive and Increased risk of miscarriage

ASRM Practice Committee. Fertil Steril 117: 53-63, 2022.

Fertility Treatments: Male + Ovulatory Factor
Ovulation Induction with Intrauterine Insemination

- **Maximize every aspect of the cycle**
  - More mature eggs
  - Trigger shot to boost ovulatory signal
  - Higher concentrations of sperm
  - Sperm placed “Upstream” past cervix
  - Progesterone support



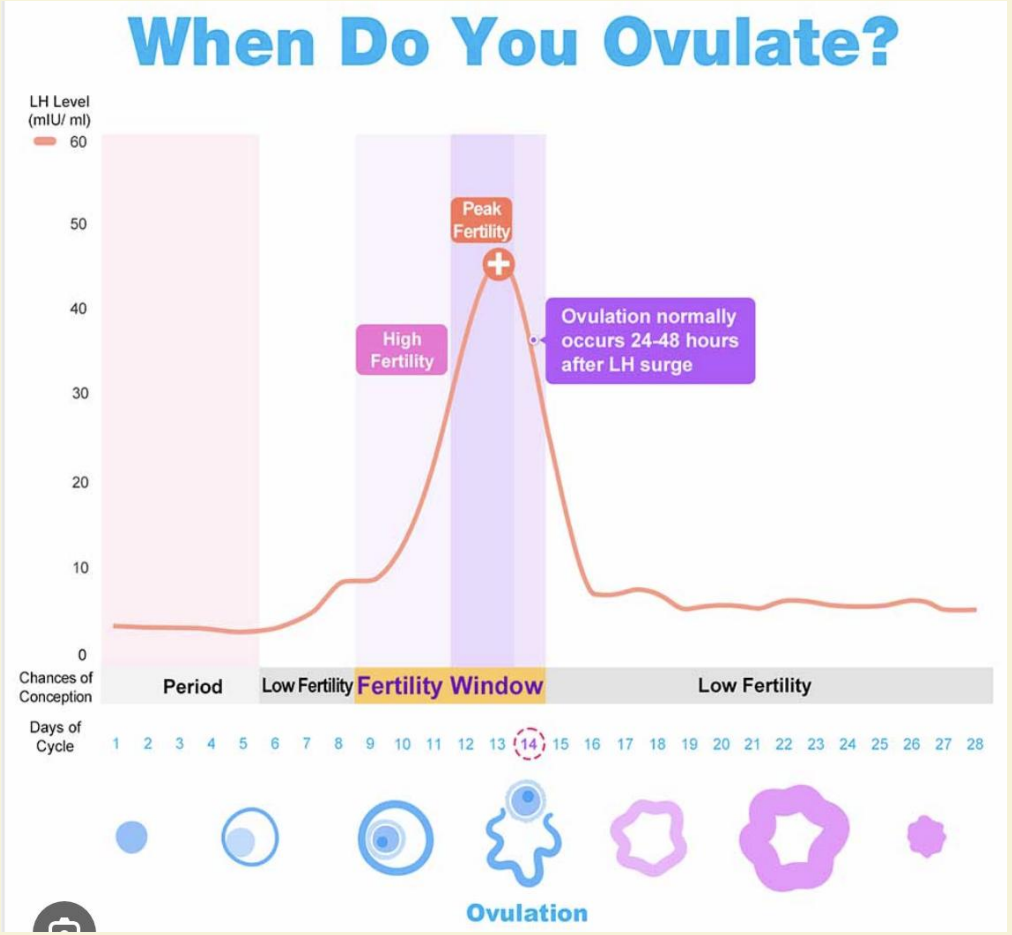
SIMPLE IUI TREATMENT PROTOCOL
(For patients that ovulate)

- **Monitoring and Timing are important**
  - Day 1 – Call with start of menses
  - Days 3 to 7-Take letrozole 2.5 mg po daily
  - Days 10 to 20 – check 2nd urine of the day for LH (Premom ovulation kits from Amazon)

  ~ Day 14 (12 to 16) -Morning of LH surge- call office to schedule IUI

  ~ Day 15 morning - perform IUI (if < 10 million total motile sperm)

  ~ Day 18 – start vaginal progesterone support
  - Day 28 to 32 – pregnancy test if no menses



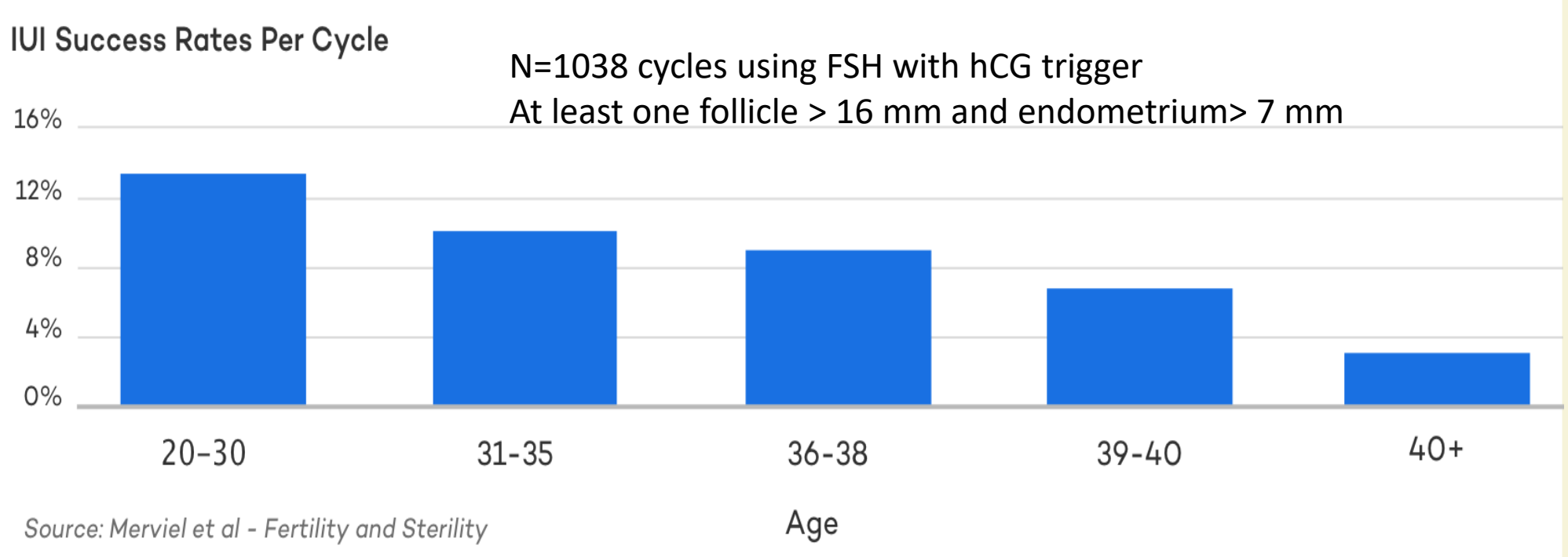
COMPLEX IUI TREATMENT PROTOCOL
(For patients that don't ovulate)

- **Monitoring and Timing are important**
  - Day 1 – Call with start of menses
  - Days 3 to 7-Take letrozole 2.5 mg po daily
  - Days 5 to 12- add low dose FSH if needed
  - Day 12 –come in for vaginal sonogram
  - Day 14 – ultrasound until 1-2 follicles >18mm
  - Day of hCG trigger 5000 IU subcutaneously
  - Within 24 hours - perform IUI

  (encourage intercourse unless < 10 million sperm

  ~ Day 18 – start vaginal progesterone support
  - Day 28 to 32 – pregnancy test if no menses

Success Rates with Ovulation Induction + IUI



- Lower success rates with other identified causes of infertility
  - Endometriosis
  - Tubal factors
  - Abnormal semen parameters

- Tobacco use
- Obesity
-pelvic adhesions

Merviel P et al. Fertil Steril 93:79-88, 2010.

What to do with Unexplained Infertility

(Ovulatory, normal HSG, normal Semen analysis, lifestyle issues addressed)

If woman is younger than 30 years old,

- try empiric clomiphene or letrozole for 3 - 4 months
- 75-90% ovulate – check progesterone
- 8-10% twins, 0.5% triplets
- 85% of pregnancies occur in first 3 ovulatory months
- 75% of pregnancies occur at with Clomid 100mg or lower or Letrozole 5 mg or lower (best for PMOS)
- Do not:
  - use supplemental estrogen until after LH surge
  - arbitrary use of hCG for ovulation triggering

When to Refer Your Patient to REI

- Female age greater than 35
- Patient of any age with low AMH (<1.0) or day 3 FSH > 10
- Severe or bilateral tubal disease
- Abnormal semen analysis
- Infertility with multiple etiologies
- Young patient with infertility of more than 24 months
- No success after 4 to 6 months of ovulation induction
- Patient frustration or expectation level is high

Summary: Algorithm for the Evaluation of Infertility