Fertile Health

Female Infertility

Monica Moore, MSN, RNC

©Fertile Health, LLC

Objectives

- Describe female anatomy and basic female reproductive function.
- List the major hormones involved in female reproduction.
- Describe the main causes of female infertility.
- Explain what happens to a woman's fertility potential as she gets older.
- Describe common diagnostic tests used to determine the causes of female fertility.
- List common treatment options available.

Diagnostic evaluation of the infertile female: a committee opinion

Practice Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

Diagnostic evaluation for infertility in women should be conducted in a systematic, expeditious, and cost-effective manner to identify all relevant factors with initial emphasis on the least invasive methods for detection of the most common causes of infertility. The purpose of this committee opinion is to provide a critical review of the current methods and procedures for the evaluation of the infertile female, and it replaces the document of the same name, last published in 2012 (Fertil Steril 2012;98:302–7).
(Fertil Steril® 2015;103:e44–50. ©2015 by American Society for Reproductive Medicine.)
Key Words: Infertility, oocyte, ovarian reserve, unexplained, conception

Earn online CME credit related to this document at www.asrm.org/elearn

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/asrmpraccom-diagnostic-evaluation-infertile-female/

Use your smartphone to scan this QR code and connect to the discussion forum for this article now.*

* Download a free QR code scanner by searching for "QR scanner" in your smartphone's app store or app marketplace.

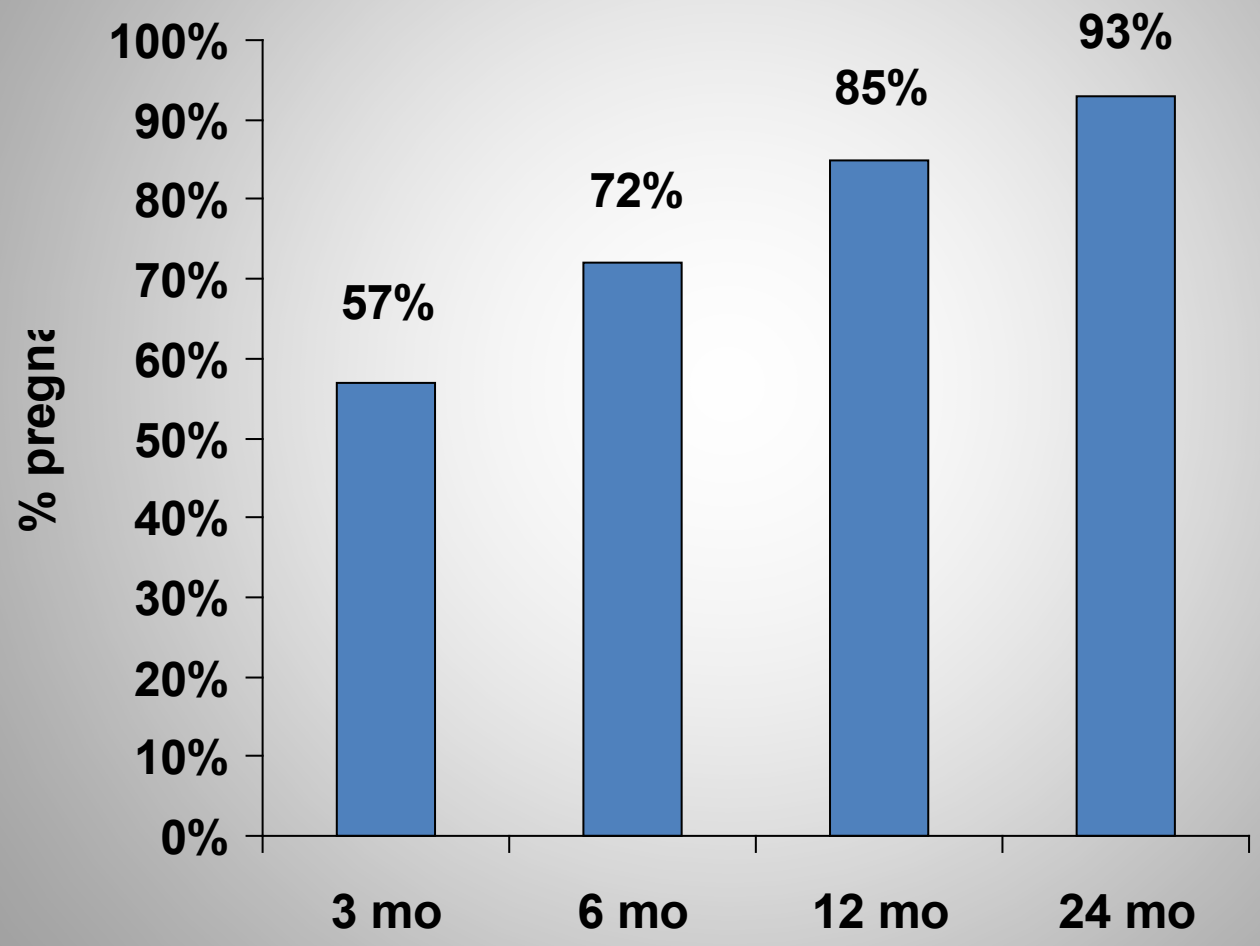
Fertil and Sterility, June 2015 (103), e44-e50.

Infertility-What is it?

- Generally defined as inability to conceive a child after one year of unprotected intercourse
  - Approx 85% of couples will achieve pregnancy within this time interval
- Earlier evaluation in women:
  - Over 35 years
  - History of oligo/amenorrhea
  - Known or suspected uterine/tubal disease or stage III-IV endometriosis
  - Known or suspected male subfertility

Practice Committee of ASRM. Fertil Steril 2015(103) e44-e50.

Time to Conception

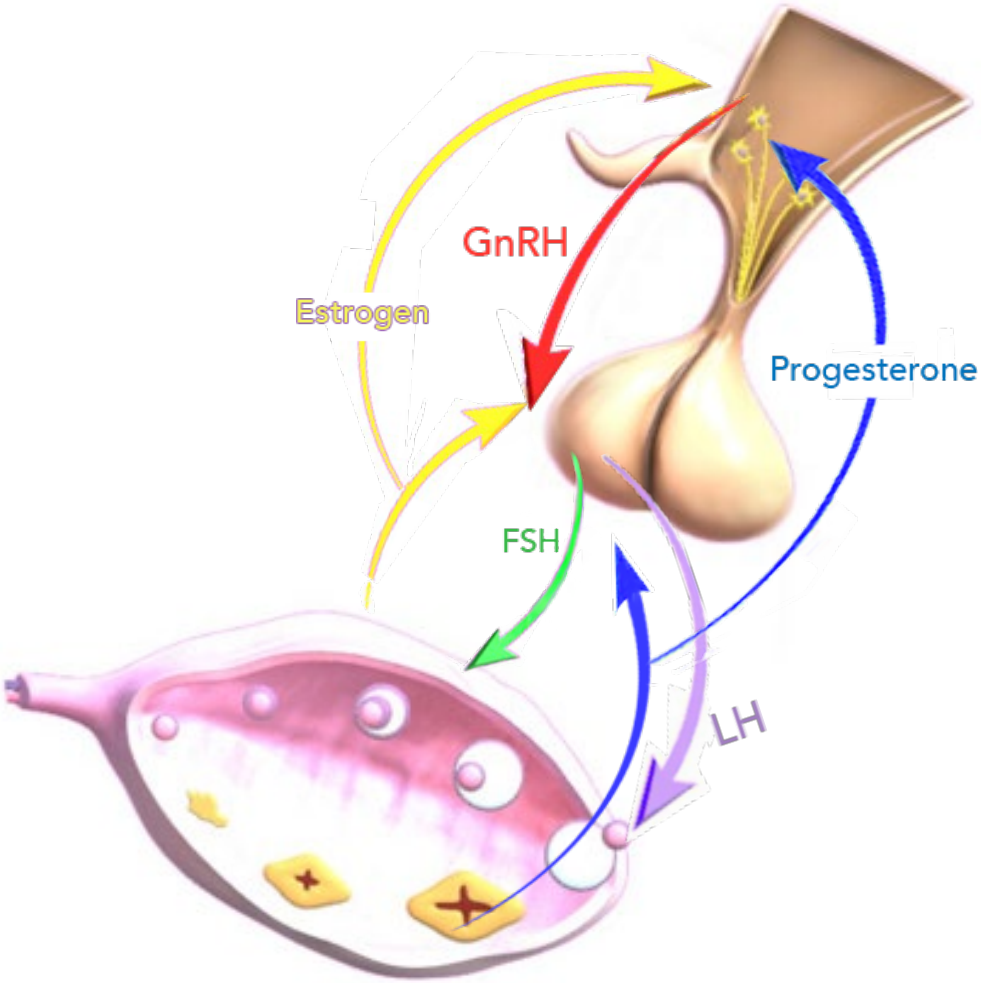


Speroff L, Glass RH, Kase NG, editors. Clinical Gynecologic Endocrinology and Infertility. 7th ed. Baltimore Williams & Wilkins, 2005

Female Fertility-Basic Principles

- HPO Axis needs to be functioning properly
- Uterus needs to be receptive to hormonal stimulation and implantation
  - Cervix needs to "allow" entry of sperm (and prevent bacteria from entering uterus)
- Ovaries need to have viable follicles that respond to hormonal stimulation and ovulate
  - If not doing IVF, fallopian tube(s) need to be patent

OVULATORY FACTOR


GnRH
Estrogen
Progesterone
FSH
LH

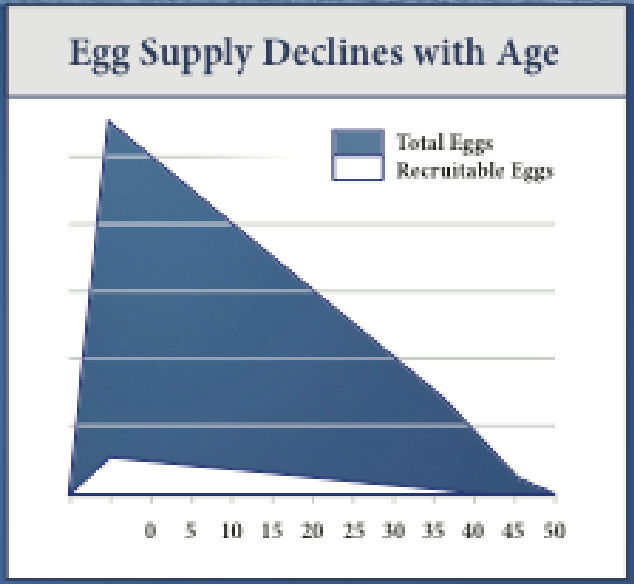
Common Types of Ovulatory Dysfunction

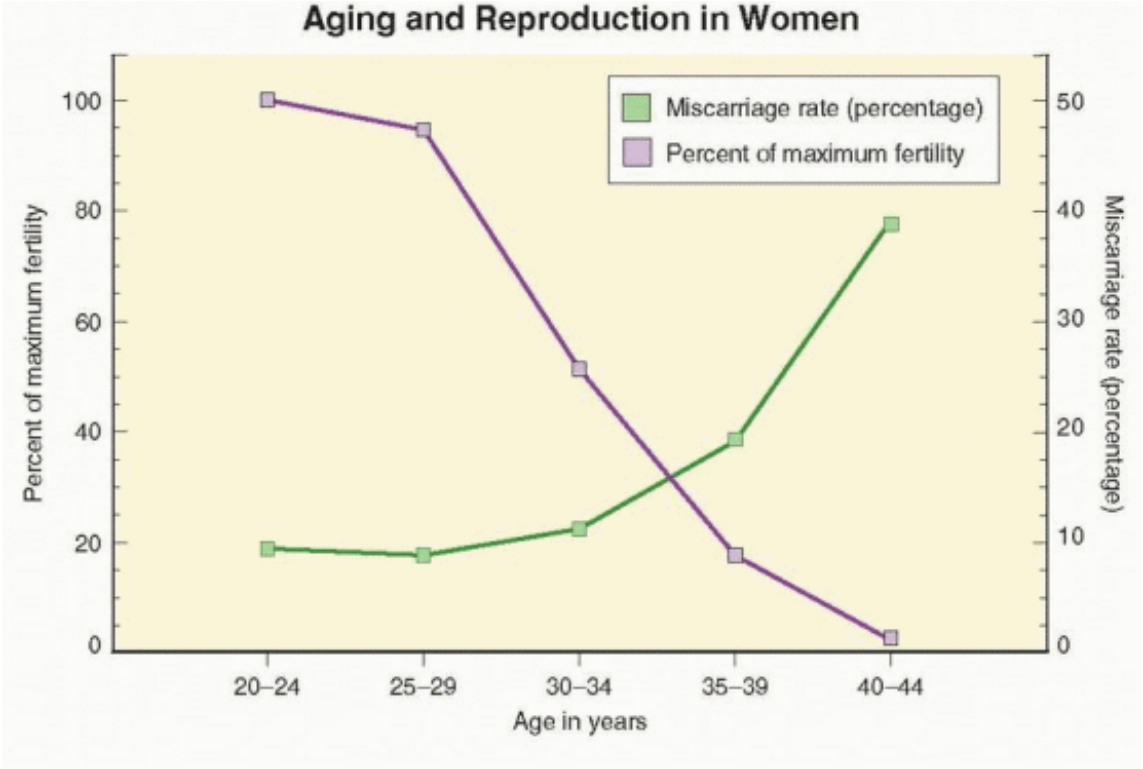
- Hypothyroidism
- Hyperprolactinemia
- Hypogonadism
  - Hyper- and Hypo-
- Ovulatory Dysfunction with Hirsutism
  - PCOS
  - CAH

IMPACT OF AGE ON FERTILITY

“Recruitable” Eggs-Egg Supply Declines with Age.

Reproductive Aging





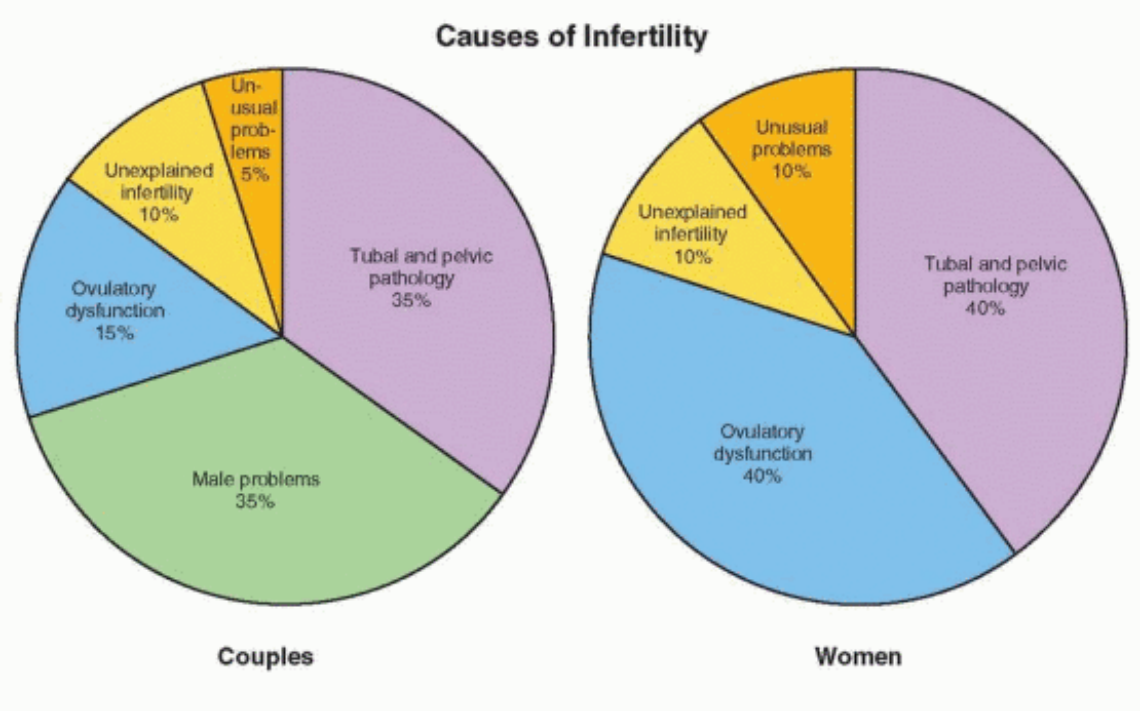
Fritz, Marc A.; Speroff, Leon
Title: ***Clinical Gynecologic Endocrinology and Infertility, 8th Edition***
Copyright ©2011 Lippincott Williams & Wilkins

Cytoplasmic Aging

- Maternal environment (particularly aging) has strong impact on the quality of cytoplasmic maturation and success of IVF
  - Mitochondria are a critical example-cell division is ‘hard work’

CAUSES OF INFERTILITY

Causes of Infertility



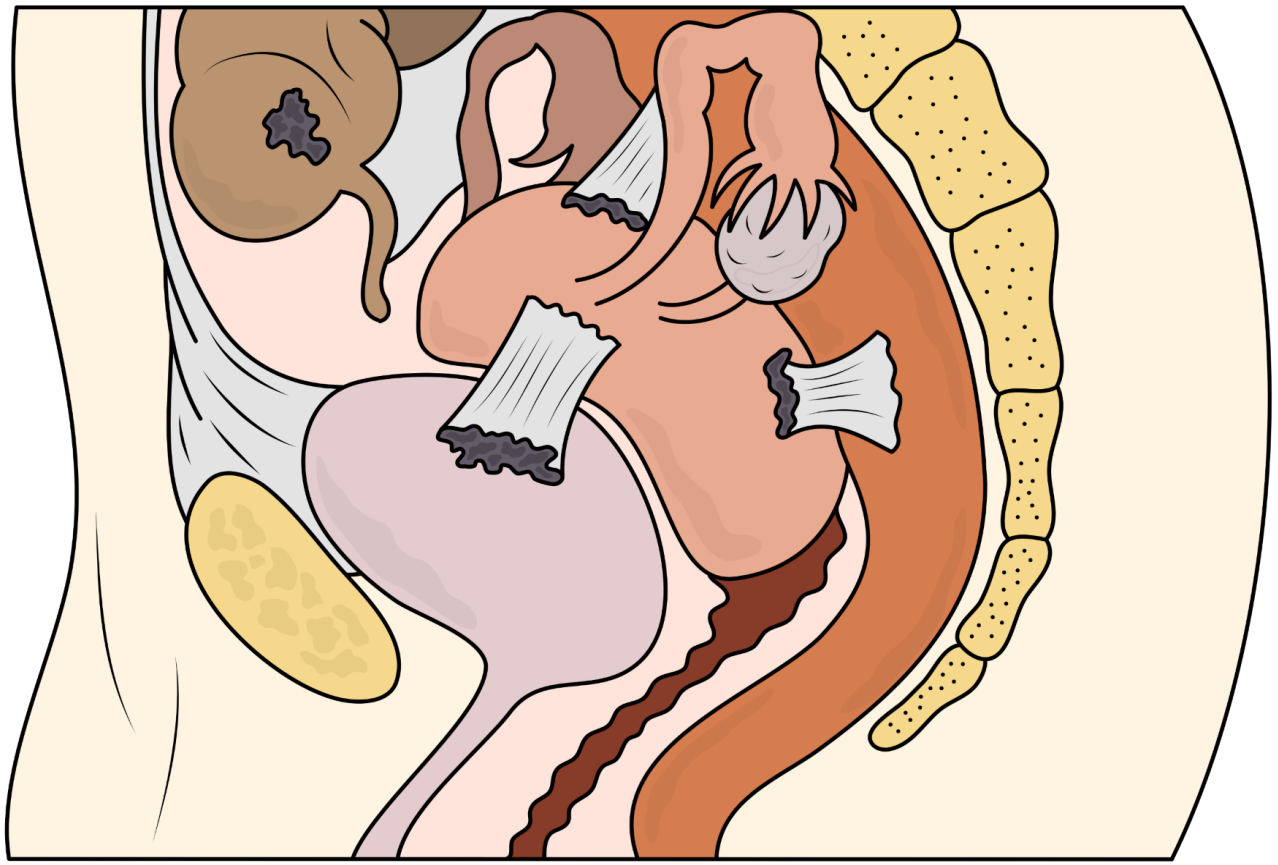
Fritz, Marc A.; Speroff, Leon
Title: ***Clinical Gynecologic Endocrinology and Infertility, 8th Edition***
Copyright ©2011 Lippincott Williams & Wilkins

PELVIC FACTORS

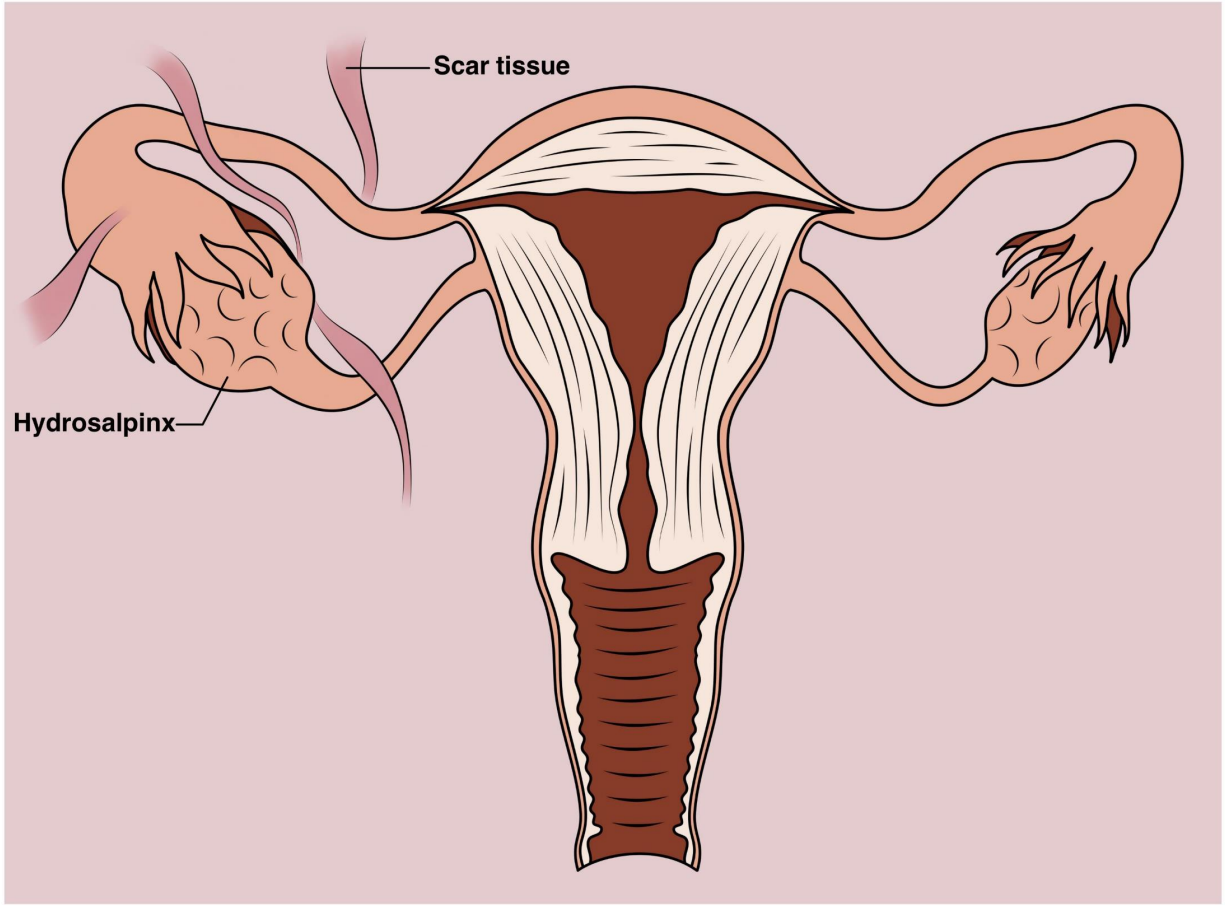
Endometriosis

- Parts of endometrium migrate to other areas in pelvis and still respond to hormones, but are “stuck”: can’t exit body.
  - Cause inflammation, pain, subfertility
- Distortion of anatomy. “Toxic” substances in pelvis
- No cure, tx options to relieve symptoms and prevent damage.
- Continuous OCPs, aromatase inhibitors, GnRH agonists (create a hypoestrogenic state)
  - Stop ovulation and alleviate pain
- Laser ablation and resection of Stage 3 and 4 (grading system correlates with disease severity, not pain level)
- Stage 1 and 2: Either Clomiphene / IUI or laser ablation (similar pregnancy rates)

Endometriosis



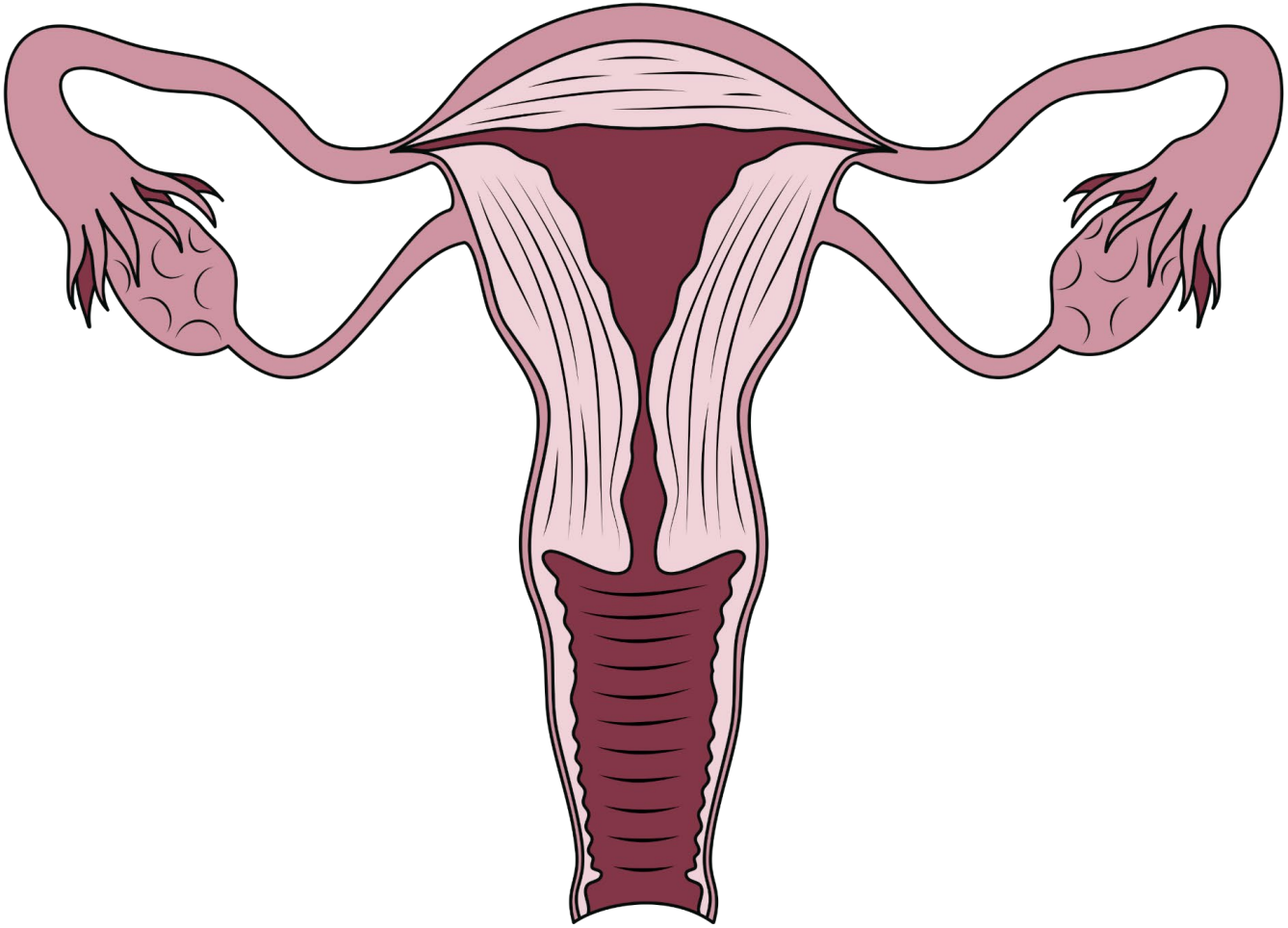
Hydrosalpinx and Scar Tissue



UTERINE FACTOR

Uterine Factor

- Anatomic and Functional Abnormalities
- Relatively uncommon cause of infertility
  - Congenital malformations
  - Leiomyomas
  - Intrauterine adhesions
  - Polyps?
  - Chronic endometritis



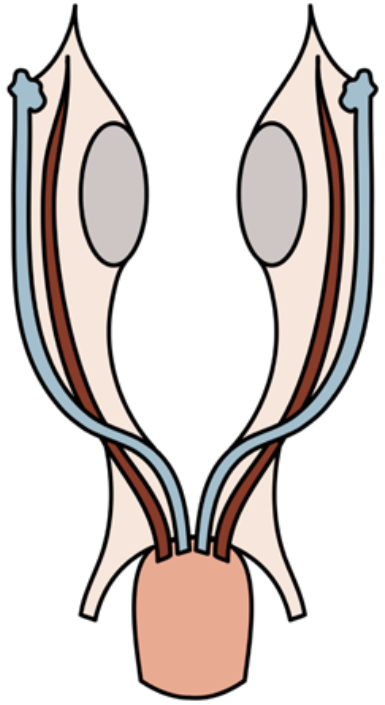
CONGENITAL UTERINE ANOMALIES

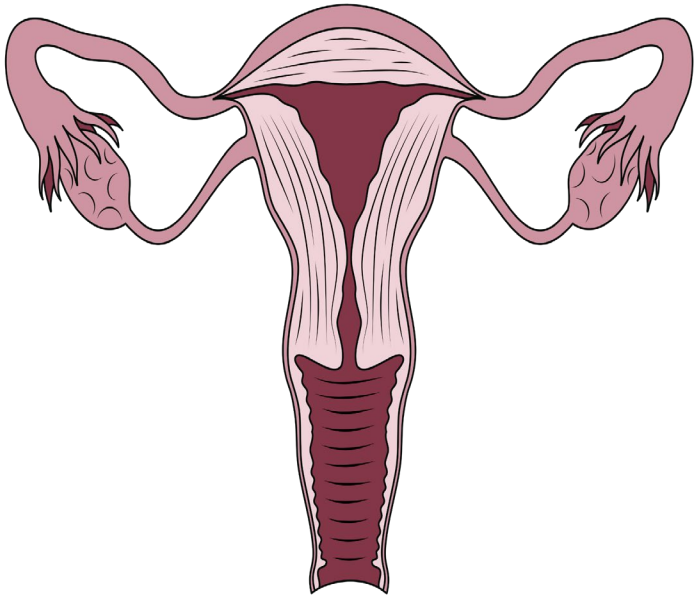
Congenital Uterine Anomalies

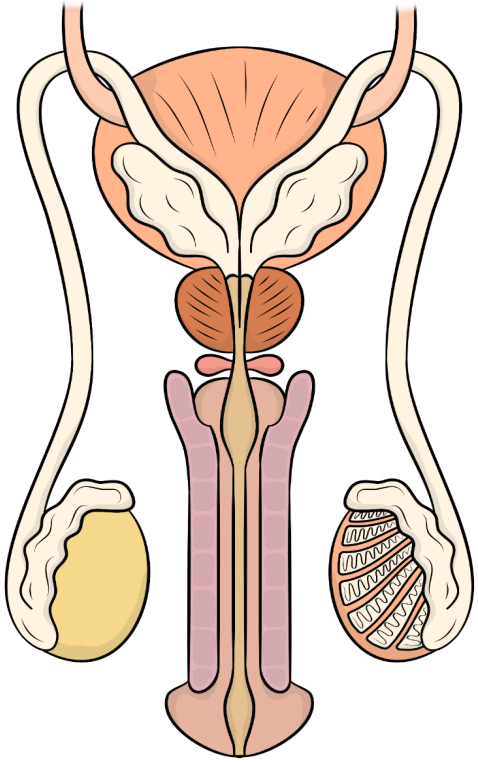
- Associated with pregnancy loss and OB complications
- Prevalence in infertile women is low, 2-4%
  - Higher (10-15%) in women with RPL
- Septate most common (35%) then bicornate (26%) arcuate (18%) and didelphys (8%).
  - In septate uterus, live birth rates can be dramatically improved after surgery

Uterine Development

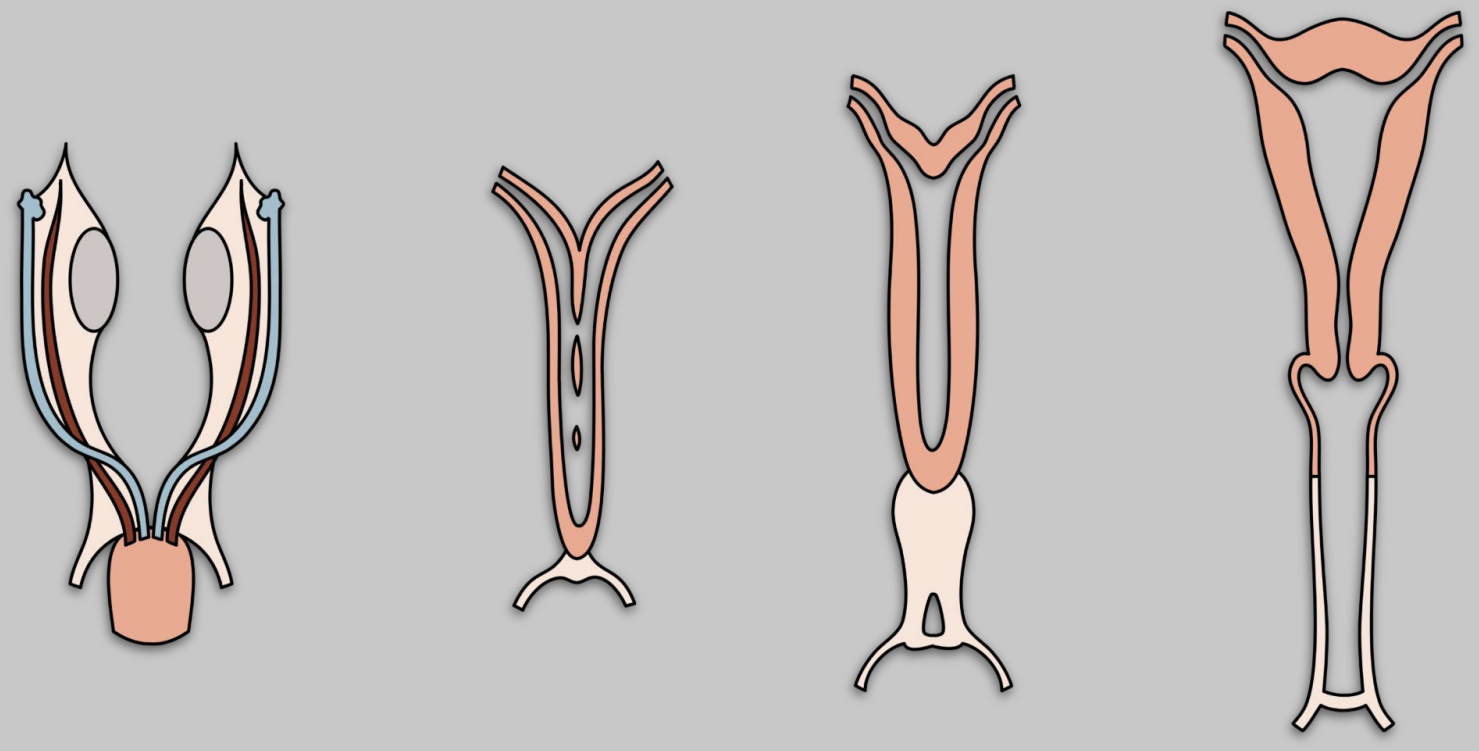
- At 5-6 weeks of development, both female and male embryos have 2 sets of paired genital ducts: mullerian and wolffian
  - Genital system identical at this point. Development depends on presence or absence of Y chromosome

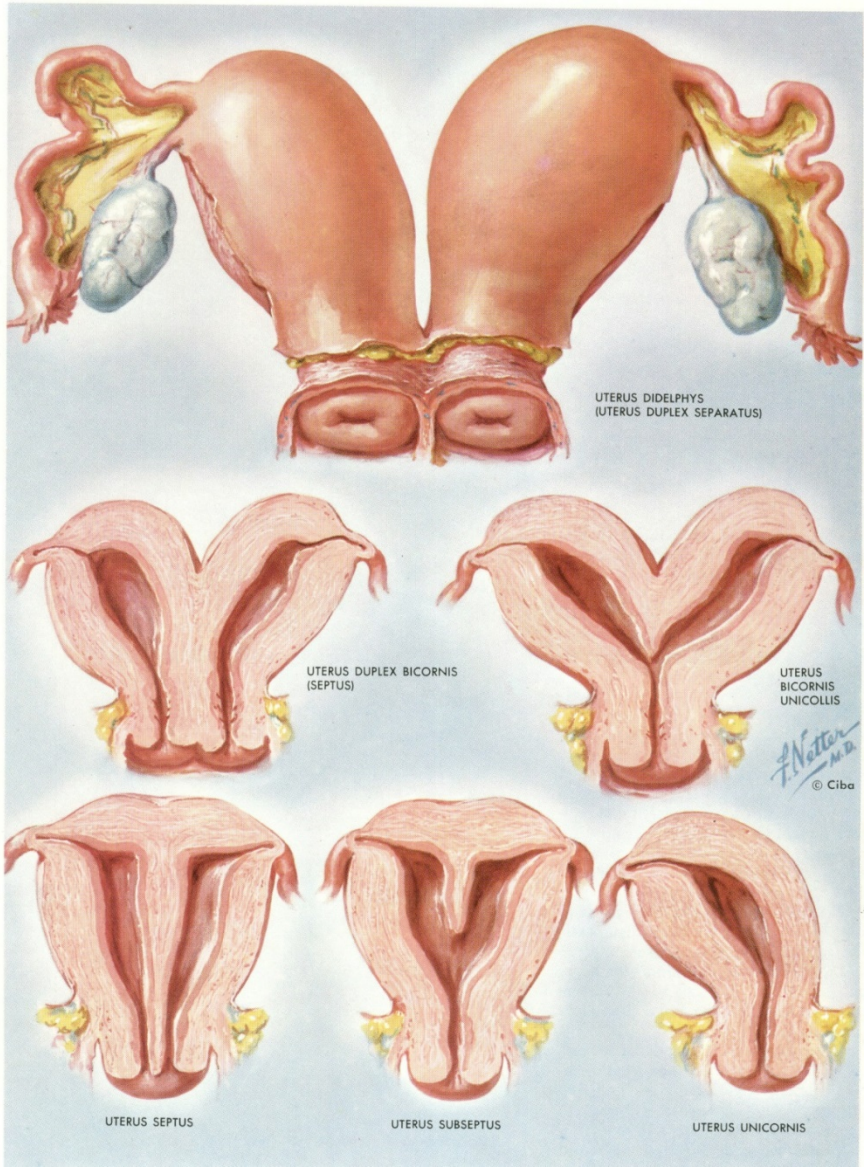






Uterine Development




UTERUS DIDELPHYS
(UTERUS DUPLEX SEPARATUS)
UTERUS DUPLEX BICORNIS
(SEPTUS)
UTERUS
BICORNIS
UNICOLLIS
F. Netter M.D.
© Ciba
UTERUS SEPTUS
UTERUS SUBSEPTUS
UTERUS UNICORNIS

Uterine Septum

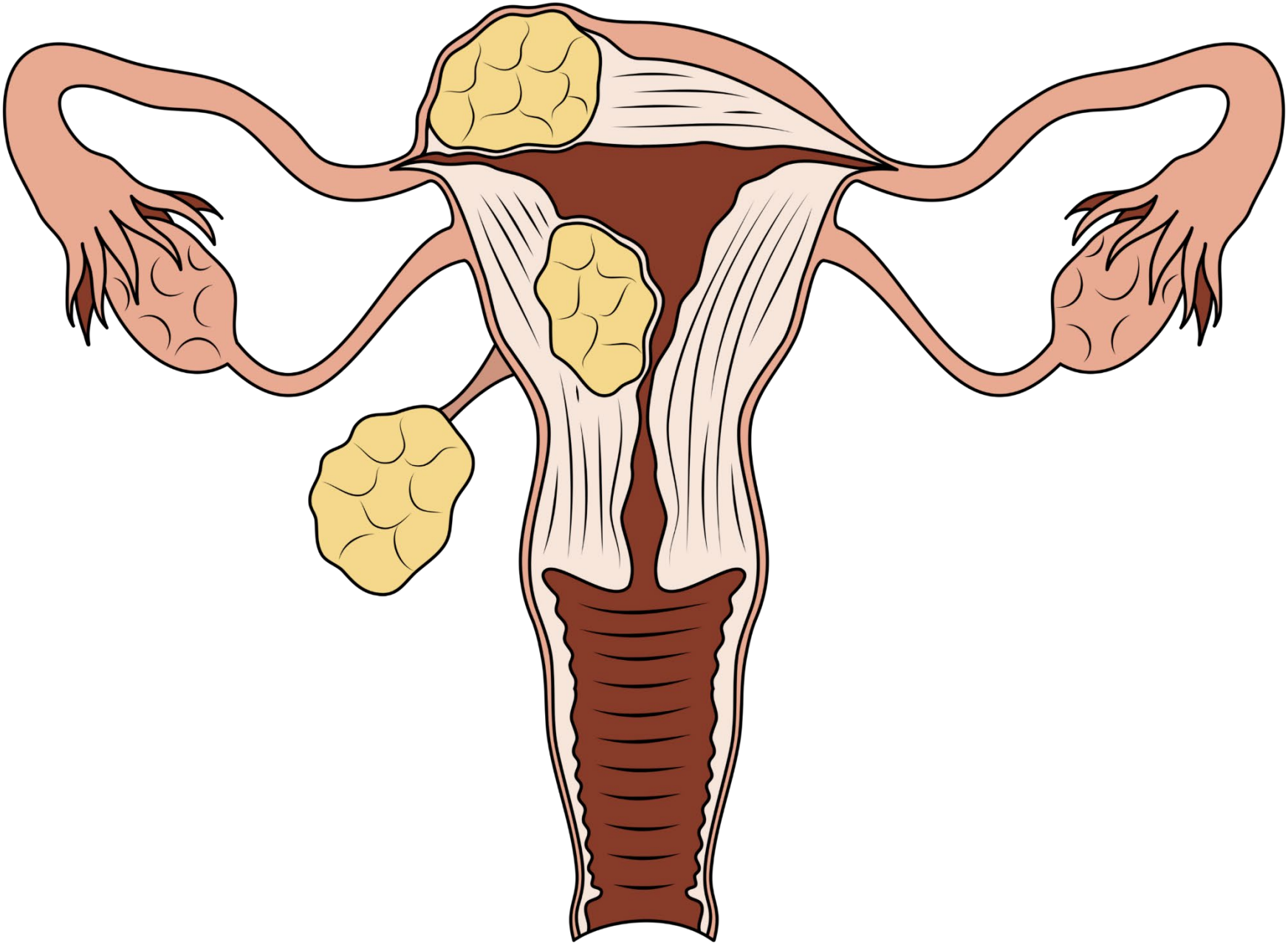
- 1-3% of all women
- 15% with renal anomaly
- Term pregnancy 20-30 % when complete septum in place

Raga et al., Hum Reprod 1993

ACQUIRED UTERINE ABNORMALITES

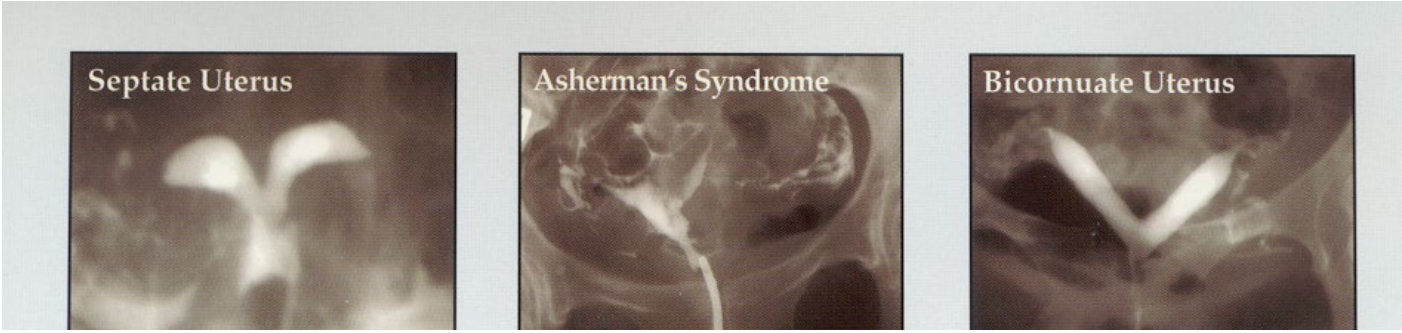
Uterine Myomas

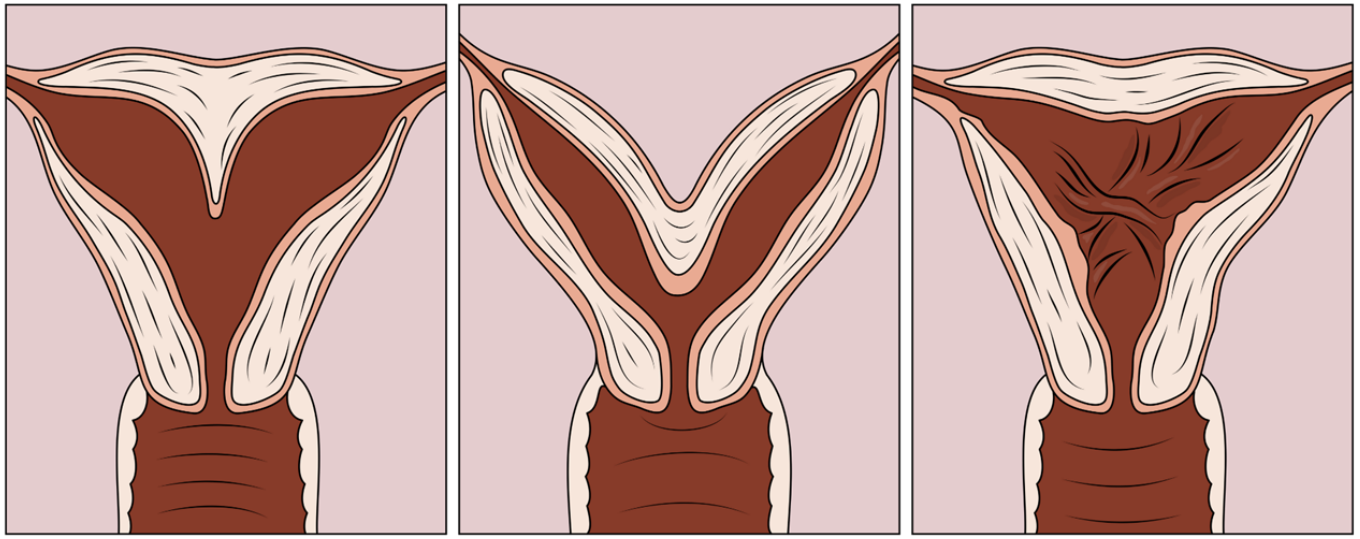
- Found in 5-10% of infertile women
- Cause of bleeding, pain and pressure, impact on fertility harder to define.
  - Enlargement or deformity of the uterine cavity (inhibiting sperm or embryo transport)
  - Obstruction of fallopian tubes
  - Distorted adnexal anatomy
  - Impaired uterine blood flow or chronic endometritis (interferes with implantation)
- Submucosal fibroids most significant adverse effect on clinical pregnancy rates.
  - Might reduce IVF rates by up to 70%



Asherman's Syndrome

- Intrauterine adhesions that result from trauma, inflammation and/or infection
- Hysteroscopy best for dx and tx
  - Misoprostol for cervical softening
  - Adhesions are lysed
  - Need physical barrier to keep uterine lining edges separated while healing
  - Cyclic HRT to re-epithelialize lining and reduce risk of recurrent adhesions


Septate Uterus
Asherman's Syndrome
Bicornuate Uterus



Endometrial Polyps

- Endometrial growths
- Increase in incidence with age
- Prevalence in infertile women 3-10%
- Polypectomy indicated when women symptomatic
- Polypectomy may improve fertility depending on size of polyp

Chronic Endometritis

- Chronic inflammation of the endometrium
  - May hinder implantation
- Associated with chlamydia and mycoplasma infections
  - Chronic retained POC?
- Diagnosis made histologically by doing endo bx
  - Presence of plasma cells
- Treated with antibiotics

TUBAL FACTOR

Tubal Factor

- One of most common causes of infertility, found in approx. 30-35% of infertile women
- H/o PID, septic abortion, ruptured appendix, tubal surgery or ectopic pregnancy suggestive of tubal damage
- Distortion of tubal anatomy precludes sperm/egg interaction or oocyte capture

Treatment of Tubal Factor Infertility

- IVF-treatment of choice if bilateral
  - Unless religious, ethical or financial restrictions
- Sterilization reversal
  - Conception rates 45-82% after microsurgical reversal. Risk for ectopic higher
- Distal tubal obstruction repair-separate and correct fimbria
  - Results depend on severity of disease-if mild, consider surgery. If severe, IVF logical choice
- Proximal tubal obstruction
  - Segmental resection and anastomosis is surgical tx. Outcomes vary.

Hydrosalpinx

- Substantial evidence that large hydrosalpinges adversely affect IVF outcome
- Interference with implantation? Backflow of "toxic" substances.
- In 2010, study showed that odds of achieving an ongoing pregnancy were twice as great after salpingectomy for hydrosalpinges before IVF compared to no intervention*.
  - Laparoscopic tubal occlusion also improved rates

*Johnson, N, van Voorst, S et al. Cochrane Database Syst Rev: CD002125, 2010.

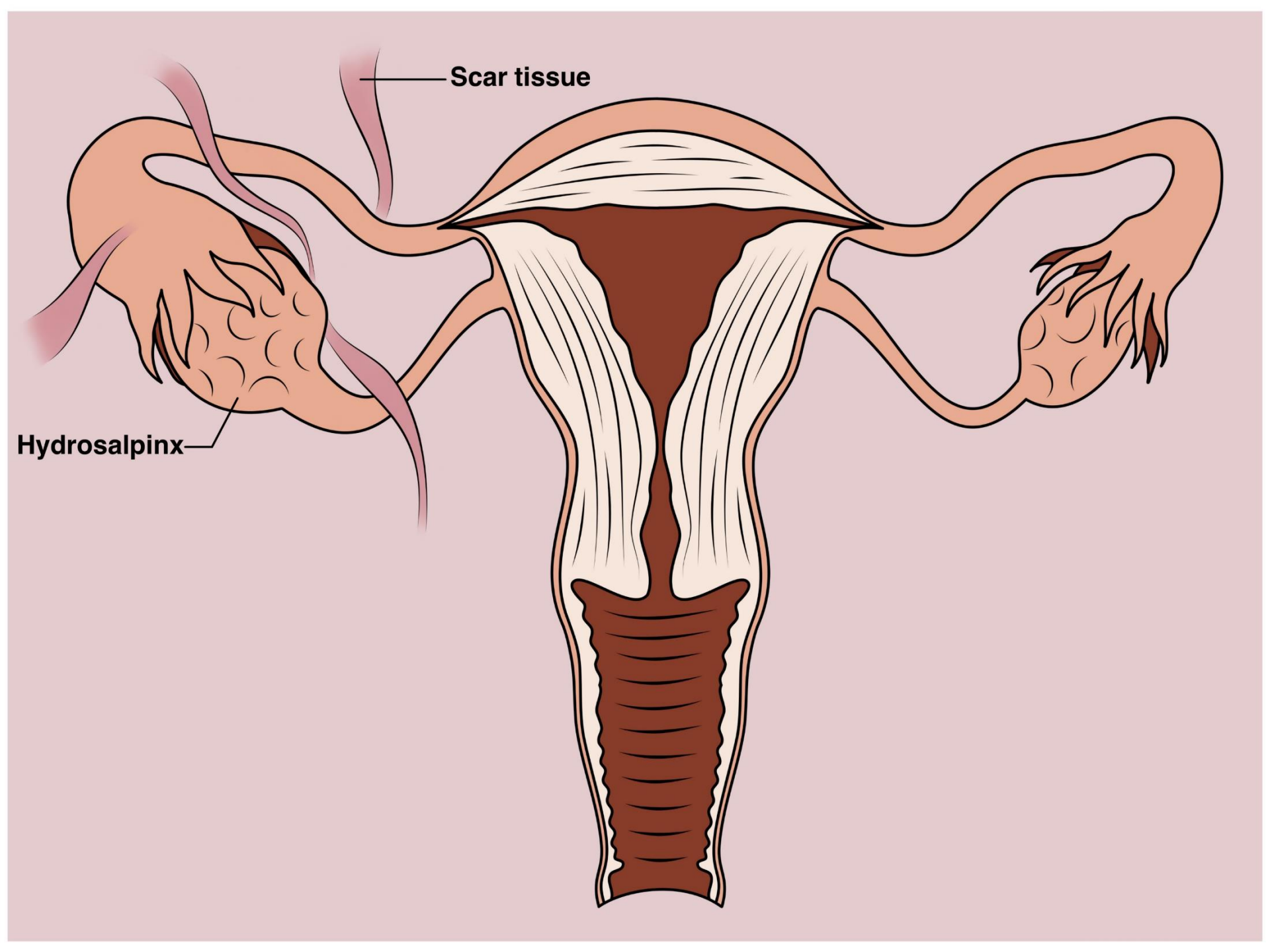

Scar tissue
Hydrosalpinx

Fig. 1. Extensive adhesions due to chlamydial infection. The right tube is affected and shows a massive hydrosalpinx

Picture from: H.-R. Tinneberg, A. Gasbarrini / International Journal of Gynecology and Obstetrics 123 (2013) S25–S30

UNEXPLAINED INFERTILITY

Unexplained Infertility

Incidence is 10-30%

Diagnosis of exclusion

- Implies normal S/A, ovulatory function, normal uterine cavity and bilateral tubal patency
- Might be subtle egg quality issue? Natural decline in fertility in female partner

Laparoscopy no longer routinely done

Treatments are empiric

- Increase number of oocytes (superovulation) and correct timing of egg/sperm interaction (IUI or IVF)

Assisted Reproductive Technology

- Both somewhat diagnostic and therapeutic for unexplained infertility
  - Able to visualize sperm, oocytes and fertilization rate
- Clearly most effective treatment for couples with unexplained infertility
  - 25-45% success rate
- ART with CCS
  - Most likely cause of unexplained infertility may relate to abnormalities in gametes or implantation

FERTILITY TESTING

ASRM Fertility Evaluation Guiding Principles

- Timing and extent of evaluation depends on
  - Patient age
  - Duration of infertility
  - Physical exam
  - Medical history
  - Patient's wishes

Fertility and Sterility, June 2015 (103), e44-e50.

History

- Duration of infertility and results of any previous eval/tx
- Menstrual history
- Pregnancy history
- Previous methods of contraception
- Coital frequency and sexual dysfunction
- Past surgery, procedures, previous hospitalizations, serious illnesses, PID or h/o STDs
- Thyroid disease, galactorrhea, hirsutism, pelvic or abdominal pain, dyspareunia
- Previous abnormal pap smears and any subsequent treatment
- Current medications and allergies
- Family history of birth defects, developmental delay, early menopause or reproductive problems
- Occupation or exposure to known environmental hazards
- Use of tobacco, alcohol, and recreational or illicit drugs

Fertil and Sterility, June 2015 (103), e44-e50.

Physical Exam

- BMI, BP, pulse
- Thyroid enlargement and presence of any nodules or tenderness
- Breast characteristics and evaluation for secretions
- Signs of androgen excess
- Vaginal or cervical abnormality, secretions or discharge
- Pelvic or abdominal tenderness, organ enlargement or masses
- Uterine size, shape, position and mobility
- Adnexal masses or tenderness
- Cul de sac masses, tenderness or nodularity

Fertil and Sterility, June 2015 (103), e44-e50

Ovarian Reserve Testing

1

"Ovarian reserve" is a function of the number and quality of oocytes

- Testing reflective of quantity; quality mostly influenced by age

2

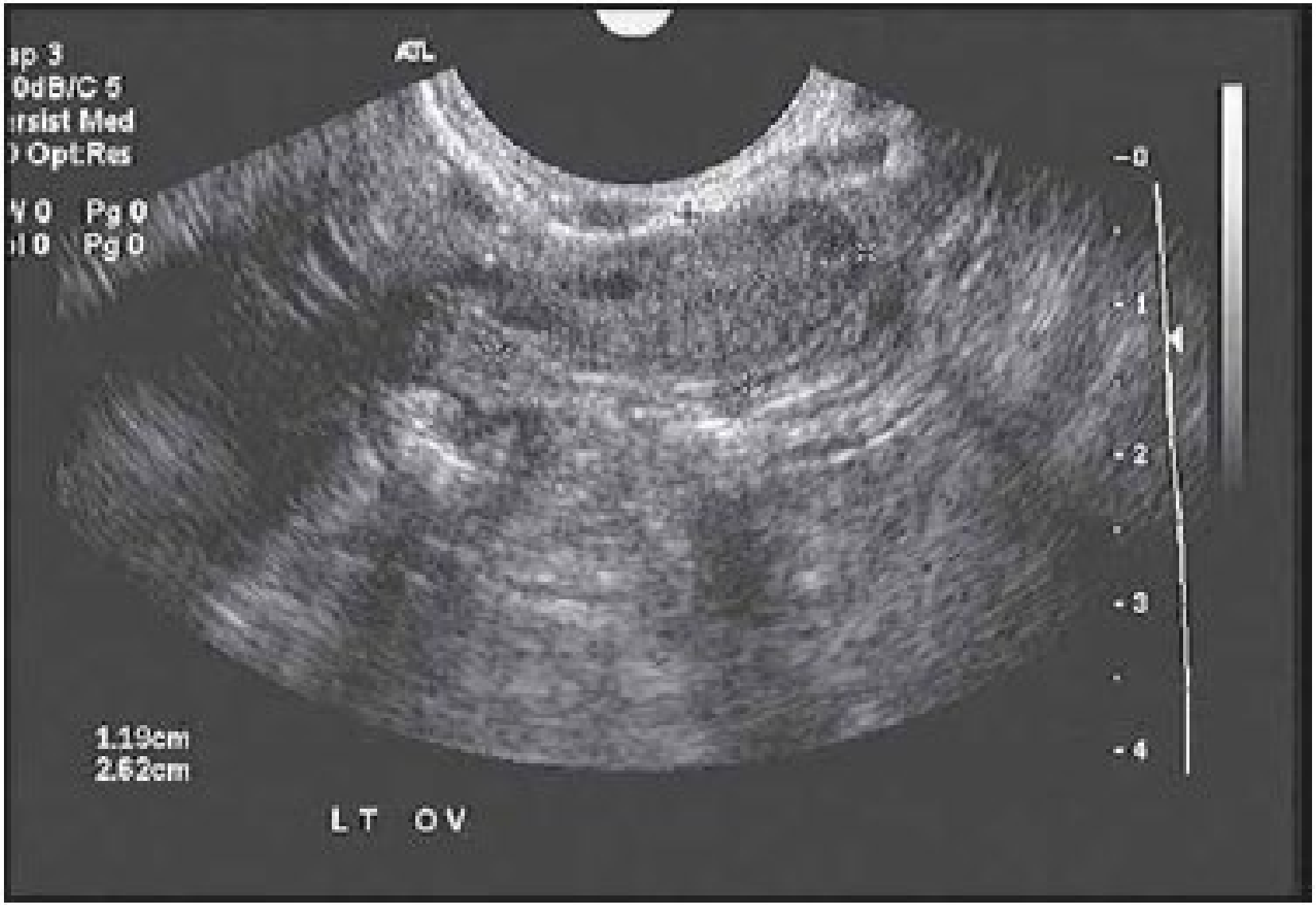
Basal (day 2-4) FSH and estradiol and BAFC most commonly used

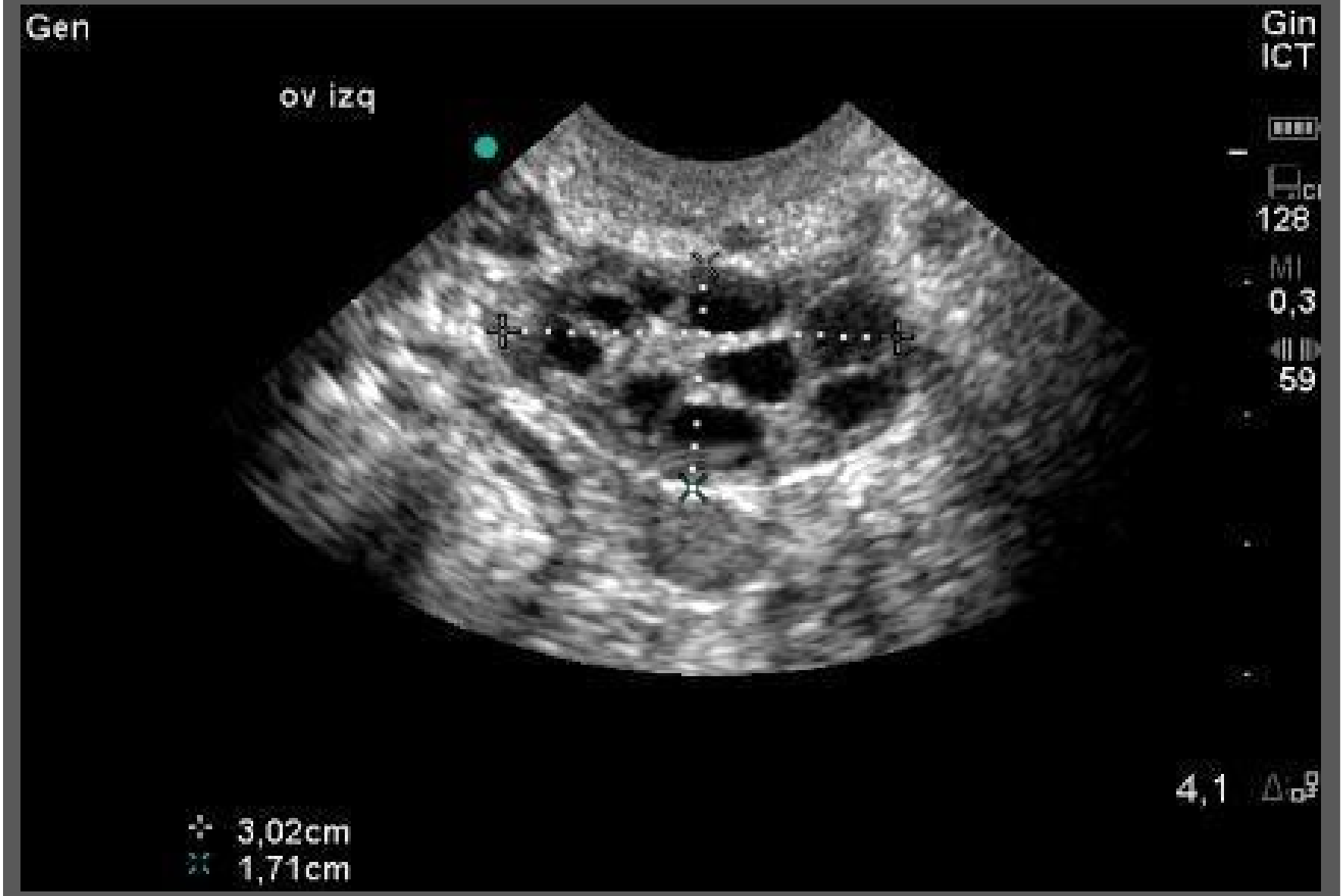
- Low BAFC –total of 3-6 follicles
- Single elevated FSH has predictive value*
- Elevated basal FSH correlated with lower overall pregnancy rates, and at IVF fewer eggs retrieved at IVF & lower pregnancy rates

3

AMH levels <1 ng/ml have been associated with poor responses to stim, poor embryo quality, and poor pregnancy outcomes in IVF.

Fert and Ster 2015 (e44-e50).

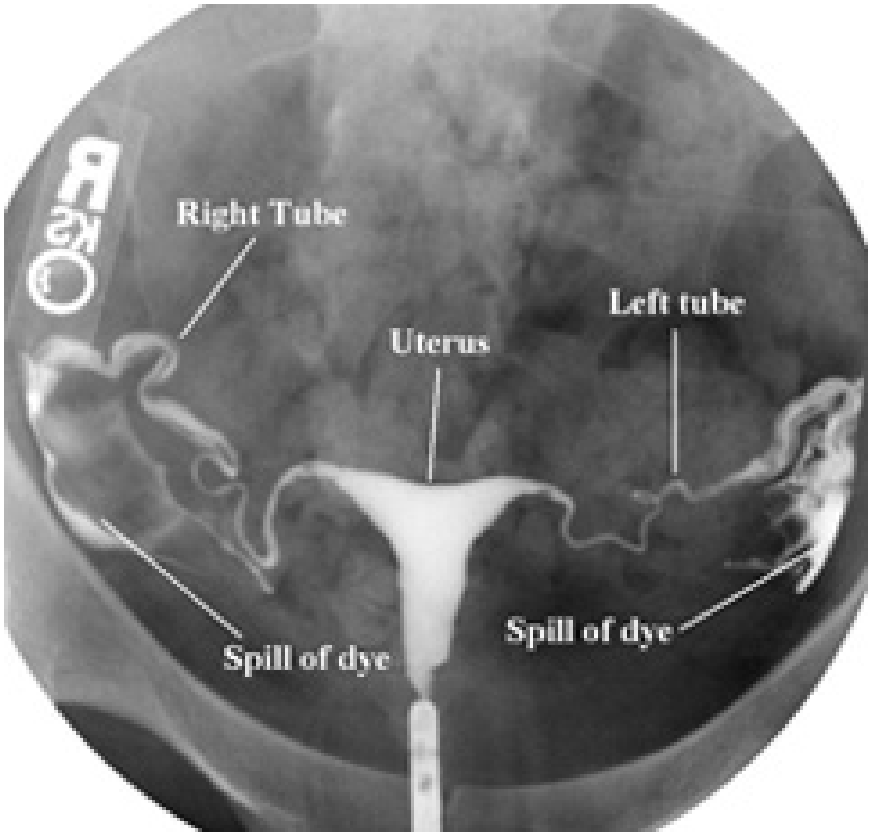

ATL
1.19cm
2.62cm
LT OV


Gen
ov izq
Gin
ICT
128
MI
0,3
59
4,1
3,02cm
1,71cm

HSG

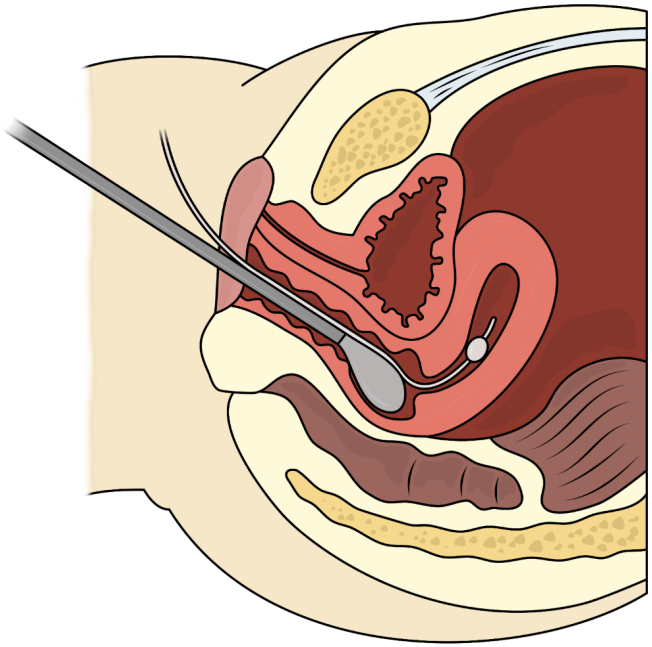
- Standard method for evaluating tubal patency
  - May offer a therapeutic benefit
  - Tubal obstruction vs tubal/uterine contractions
- Low sensitivity for uterine abnormalities
  - 50-75% sensitivity
- Also can't differentiate between some uterine abnormalities
  - i.e. septate vs bicornuate uterus.
- Laparoscopy with chromotubation (cervical injection of blue dye) can also demonstrate tubal patency
  - Can correct abnormal findings during procedure
- Tx with antibiotics (doxy 100 mg BID for 5 days starting 1-2 days prior to HSG) when tubal disease suspected, to decrease risk of acute salpingitis.

HSG

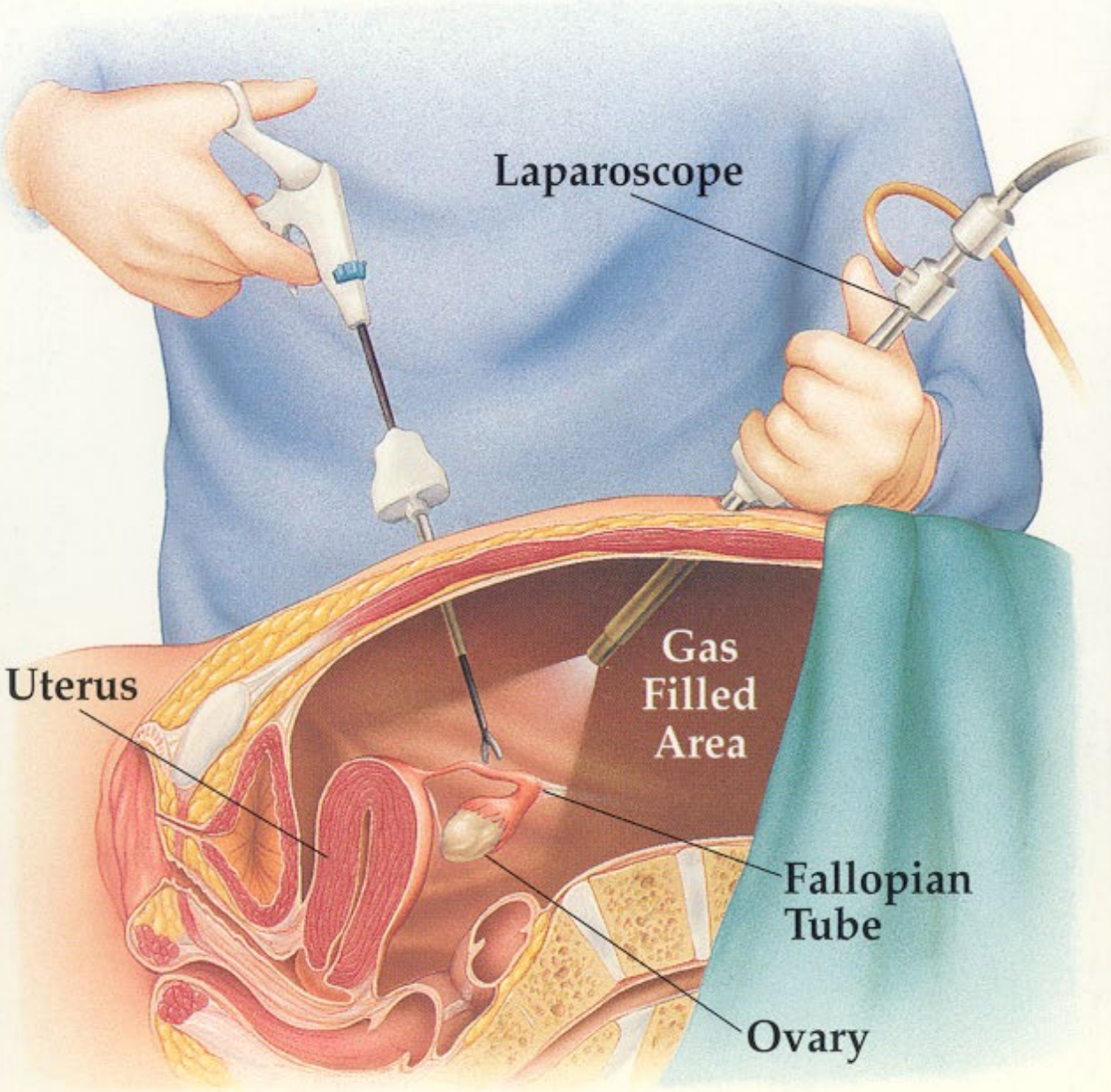


www.dallasivf.com

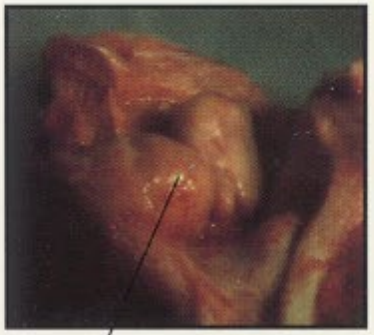
Saline Sonogram



Laparoscopic Procedure



Chocolate Cyst
(Endometriosis)



Fibroid Tumor

Pelvic Adhesions
and Scar Tissue

Conclusion

- Infertility affects 10-15% of couples
- Diagnosis, testing and treatment of infertility should be done systematically, taking into account patient age, duration of fertility and other pertinent factors (ethical and financial constraints).
- The advances of ART have increased success rates in couples with unexplained fertility.

QUESTION AND ANSWER SECTION

Female Infertility Questions

- In terms of female fertility, what three structures/organs needs to be functioning properly:
- HPO Axis, Uterus, Ovaries/tubes
- Name two of the most common causes of ovulatory infertility:
- Hypothyroidism, Hyperprolactinemia, PCOS

- When is the time in a woman's life when she has the most eggs/follicles?
- After what age do we see a rapid decline in egg quality?
- The most common reason for the decrease in fertility potential and increase in miscarriage rate (with age) is: _____.
- What structure in the cytoplasm (as it ages) can contribute to a decrease in efficiency of cell division?

- Name two ways that endometriosis can contribute to infertility?
- What are three common treatments to manage endometriosis?
- The best way to achieve pregnancy with stage 3-4 endometriosis is:

- Congenital uterine anomalies are most associate with: Infertility or pregnancy loss (choose 1)
- _____ fibroids have the most significant effect on clinical pregnancy rates
- What is the name of the condition associated with uterine adhesions, most commonly as a result of uterine surgery/instrumentation?

- A septate and a bicornuate uterus look similar on HSG, true or false?
- A woman with a h/o chlamydia is more at risk for what 2 things?
- The best way to achieve a pregnancy with a hydrosalpinx is with IVF, true or false?
- The best test to look at the uterine cavity is:

- What would you expect the clinician to do prior to HSG if he/she suspects that the patient has tubal disease?
- How do you diagnose endometriosis?