



UpTo Date
2021

Female Infertility

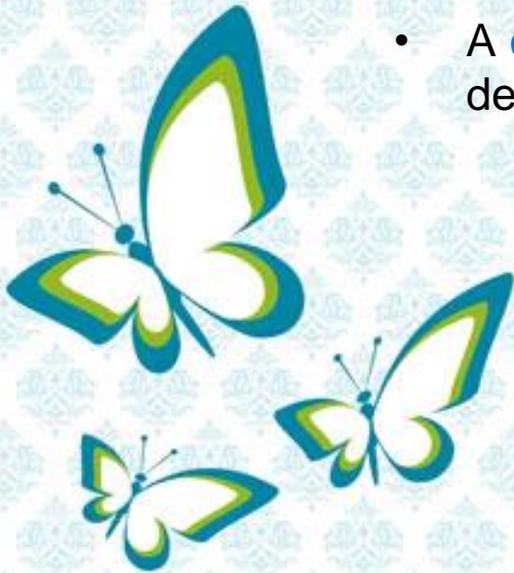


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Infertility Fellowship

- An infertility evaluation is usually initiated after **one year** of regular unprotected intercourse in women **under age 35 years** and after **six months** in women age ≥ 35 years .
- The evaluation may be initiated **sooner** in women with :
 - irregular menstrual cycles ,
 - known risk factors for infertility (endometriosis, a history of PID , or reproductive tract malformations).
- A **complete initial diagnostic evaluation** should be performed to detect the most common causes of infertility .



CAUSES OF INFERTILITY

- Male factor – 26 %
- Ovulatory dysfunction – 21 %
- Tubal damage – 14 %
- Endometriosis – 6 %
- Coital problems – 6 %
- Cervical factor – 3 %
- Unexplained – 28 %



CAUSES OF FEMALE INFERTILITY

- Ovulatory disorders - 25 %
- Endometriosis - 15 %
- Pelvic adhesions - 12 %
- Tubal blockage - 11 %
- Other tubal abnormalities - 11 %
- Hyperprolactinemia - 7 %



OVARY

- Ovulatory disorders :
(oligoovulation or anovulation) results in infertility because an oocyte is not available every month for fertilization
- Oocyte aging :
is an important factor affecting a woman's fertility due to a decline in both the quantity and quality of the oocytes
- Ovarian cysts :
it is **unclear** whether small (< 3 - 6 cm) ovarian cysts have a role in infertility and that the effects of surgical treatment are often more harmful than the cyst itself to the ovarian reserve



Causes of ovulatory dysfunction

Primary hypothalamic-pituitary dysfunction

Immaturity at onset of menarche or perimenopausal decline

Intense exercise

Eating disorders

Stress

Idiopathic hypogonadotropic hypogonadism

Hyperprolactinemia

Lactational amenorrhea

Pituitary adenoma or other pituitary tumors

Kallman syndrome

Tumors, trauma, or radiation of the hypothalamic or pituitary area

Sheehan's syndrome

Empty sella syndrome

Lymphocytic hypophysitis (autoimmune diseases)

Other disorders

Polycystic ovary syndrome

Hyperthyroidism or hypothyroidism

Hormone-producing tumors (adrenal, ovarian)

Chronic liver or renal disease

Cushing's disease

Congenital adrenal hyperplasia

Premature ovarian failure, which may be autoimmune, genetic, surgical idiopathic, or related to drugs or radiation

Turner syndrome

Androgen insensitivity syndrome

Medications

Estrogen-progestin contraceptives

Progestins

Antidepressant and antipsychotic drugs

Corticosteroids

Chemotherapeutic agents

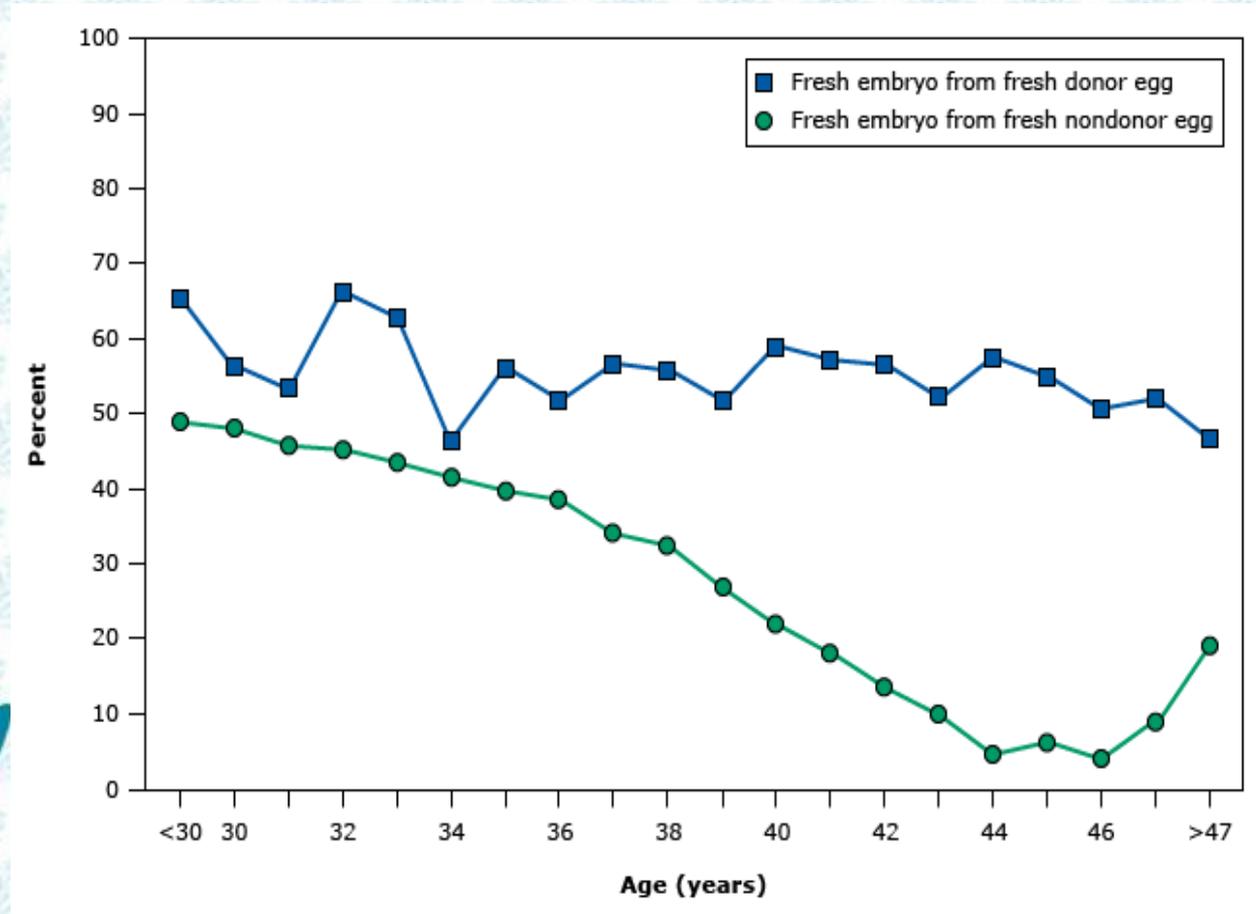


World Health Organization classification of anovulation

- class 1 – Hypogonadotropic hypogonadal anovulation is the least common, occurring in 5 to 10 % of cases. Examples of women in this category are women with hypothalamic amenorrhea from functional etiologies such as excessive exercise or low body weight.
- class 2 – Normogonadotropic normoestrogenic anovulation is the most common, accounting for 70 to 85 % of cases. Women with PCOS usually fall into this category.
- class 3 – Hypergonadotropic hypoestrogenic anovulation occurs in 10 to 30 % . Women with primary gonadal failure (previously called premature ovarian failure) or gonadal dysgenesis, comprise the majority of these cases.
- Hyperprolactinemic anovulation is a separate category; gonadotropin concentrations in this condition are usually normal or decreased.



Percentages of transfers using fresh embryos from fresh donor or fresh nondonor eggs that resulted in live births, by age of woman



FALLOPIAN TUBE ABNORMALITIES

PELVIC ADHESIONS

- prevent normal transport of the oocyte and sperm through the fallopian tube.
- The primary cause of tubal factor infertility is **PID** caused by pathogens such as **chlamydial** or **gonorrhea**.
- Other conditions that may interfere with tubal transport include severe **endometriosis** , adhesions from previous **surgery** or non tubal **infection** (eg, appendicitis, inflammatory bowel disease), pelvic tuberculosis, and salpingitis isthmica nodosa .



- Proximal tubal blockage may result from plugs of mucus and amorphous debris or spasm of the uterotubal ostium, but does not reflect true anatomic occlusion
- Women with **distal tubal obstruction** may develop hydrosalpinges, which decrease the success rate of IVF.
- In addition to obstruction to *sperm migration*, **hydrosalpinges** appear to reduce fertility by *retrograde flow* of tubal contents into the endometrial cavity, which creates a hostile environment to implantation of an embryo.
- **Removal of the hydrosalpinges increases the success of IVF.**



UTERUS

- **Impaired implantation**, either mechanical or due to reduced endometrial receptivity, are the basis of uterine causes of infertility.
- However, the impact of **fibroid** presence or removal on live birth rate is unclear.
- It appears that fibroids with a **submucosal or intracavitary** component can lower pregnancy and implantation rates .



- **Uterine abnormalities** are thought to cause infertility by interfering with normal implantation.
- Müllerian anomalies are a significant cause of recurrent pregnancy loss , with the **septate** uterus associated with the poorest reproductive outcome .
- Other structural abnormalities associated with infertility include endometrial polyps, and synechiae from prior pregnancy-related curettage.
- However, data establishing a causal link between these uterine abnormalities and infertility are lacking.



- **Luteal phase defect** (LPD) refers to abnormalities of the corpus luteum that result in inadequate production of progesterone, which is necessary for making the endometrium receptive to implantation.

- There are no agreed upon definitions, diagnostic tests, or treatments for LPD .

- *We agree that endometrial dating is not useful for evaluating or guiding treatment of infertile women .*



- **Inherited thrombophilias** do not appear to be related to unexplained infertility .
- A large retrospective study reported no significant association with common thrombophilias, including factor V Leiden and lupus anticoagulant, and diminished IVF success .
- *Neither screening for thrombophilias nor treating them is advised in cases of repeated infertility treatment failure.*



- Women with some **autoimmune diseases** are at increased risk of infertility unrelated to direct effects of these antibodies on fertilization and implantation.
- **Premature ovarian failure** has also been described in women with systemic lupus erythematosus and myasthenia gravis.
- **Autoimmune oophoritis** may occur as part of type I and type II syndromes of polyglandular autoimmune failure, which are associated with autoantibodies to multiple endocrine and other organs.



- Infertile couples have been shown to have a higher prevalence of **karyotype abnormalities** (trisomies, mosaics, translocations) than the general population .

- *The most common aneuploidies associated with infertility are 45, X (Turner syndrome) in women and 47, XXY (Klinefelter syndrome) in men.*



Evaluation



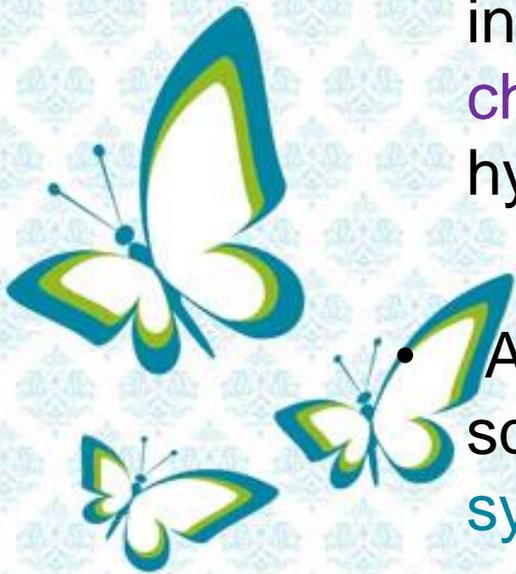
History and physical examination

Female
Duration of infertility
Number and outcome of any prior pregnancies (including ectopic and miscarriages) with the same or a different partner
Gynecologic history, including history of pelvic inflammatory disease, fibroids, endometriosis, cervical dysplasia; surgery of the cervix, ovary, uterus, fallopian tube, pelvis, or abdomen; intrauterine device use, other prior contraceptive use, diethylstilbestrol exposure in utero, uterine anomalies.
Menstrual history (age at menarche, cycle length, and regularity), presence of melasma or vasomotor symptoms (hot flashes), dysmenorrhea
Changes in hair growth, body weight, or breast discharge
Other medical and surgical history
Medications
History of chemotherapy or radiation
Cigarette smoking, alcohol, marijuana and other drug use; environmental and occupational exposures
Exercise and dietary history
Frequency of intercourse, use of lubricants (which may be toxic to sperm). Presence of deep dyspareunia suggestive of endometriosis.
Previous infertility testing and therapies
Family history of birth defects, intellectual disability, or reproductive failure
Pelvic or abdominal pain, symptoms of thyroid disease



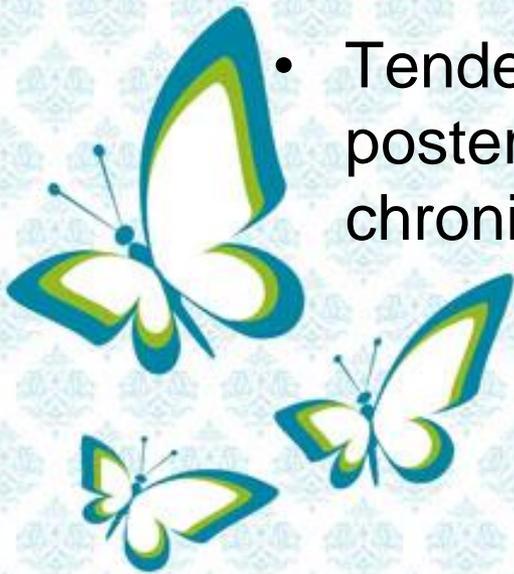
Physical examination

- The patient's **BMI** should be calculated and **fat distribution** noted, as extremes of BMI are associated with reduced fertility and abdominal obesity is associated with insulin resistance.
- In the setting of primary amenorrhea, incomplete development of **secondary sexual characteristics** is a sign of hypogonadotropic hypogonadism.
- A body habitus that is short and stocky, with a squarely shaped chest, suggests **Turner syndrome** in patients with absent periods.



- Abnormalities of the thyroid gland, galactorrhea, or signs of androgen excess (hirsutism, acne, male pattern baldness, virilization) suggest the presence of an endocrinopathy .

- Tenderness or masses in the adnexae or posterior cul-de-sac are consistent with chronic PID or endometriosis.



Diagnostic tests

- Semen analysis to detect male factor infertility.
- Documentation of normal ovulatory function.
- A test to rule out tubal occlusion and assess the uterine cavity.
- A test or tests of ovarian reserve such as cycle day 3 FSH or E2, CCCT , AMH, or AFC .



Assessment of ovulatory function

- women who have **regular menses** approximately every 28 days **with molar symptoms** prior to menses are most likely ovulatory.
- In women who do not describe their cycles as such, laboratory assessment of ovulation should be performed.
- Ovulation is most easily documented by a **mid-luteal phase serum progesterone** level, which *should be obtained approximately one week before the expected menses.*
- *A **progesterone** level $>3 \text{ ng/mL}$ is evidence of recent ovulation .*



- An alternative is to have the patient use an over-the-counter **urinary ovulation prediction kit**.
- Other methods of determining ovulation, such as daily ultrasounds to follow the development and ultimately the disappearance of a follicle .
- *If the mid-luteal progesterone concentration is <3 ng/mL, the patient is evaluated for causes of anovulation :*
 - ✓ The minimal work-up includes serum prolactin , TSH, FSH, and assessment for PCOS .



Assessment of ovarian reserve

- Diminished ovarian reserve can refer to :
 - ✓ oocyte quality, oocyte quantity, or reproductive potential
- *There is no ideal test for assessing ovarian reserve.*
- We test ovarian reserve with an AMH level and a day 3 FSH and E2 levels.
- These tests have good specificity for predicting a poor **response in IVF cycles**, but have more limited value for predicting IVF outcome.



- *With either test, a normal result is not useful in predicting fertility, but a **highly abnormal result** (FSH >15 mIU/mL) suggests that pregnancy is unlikely with treatment involving the woman's own oocytes, particularly in women of more advanced reproductive age.*
- Based on these findings and the cost advantage and simplicity of the day 3 FSH :
 - ✓ we consider a value < 10 mIU/mL suggestive of adequate ovarian reserve,
 - ✓ and levels of 10 – 15 mIU/mL borderline



- We also check a cycle day 3 E2 level, although there are conflicting data as to whether it is predictive of ovarian reserve and the response to ovarian stimulation .
- *We consider a value <80 pg/mL suggestive of adequate ovarian reserve .*
- In one prospective study of women undergoing IVF,
 - ✓ day 3 E2 levels >80 pg/mL resulted in higher cycle cancellation rates and lower pregnancy rates,
 - ✓ and E2 levels >100 pg/mL were associated with a 0 % pregnancy rate .



- **Elevated basal E2 levels** are due to advanced premature follicle recruitment that occurs in women with **poor ovarian reserve**.
- High E2 levels can **inhibit pituitary FSH production** and thus mask one of the signs of decreased ovarian reserve in **perimenopausal** women.

Thus, measurement of both FSH and estradiol levels helps to avoid false-negative FSH testing.



- **AMH** is a member of the TGF-beta family and is expressed by the small (<8 mm) preantral and early antral follicles.
- The AMH level reflects the **size** of the primordial follicle pool, and may be **the best biochemical marker of ovarian function** across an array of clinical situations .
- In adult women, AMH levels gradually decline as the primordial follicle pool declines with age ; AMH is undetectable at menopause .



- In patients planning IVF, AMH level correlates with the number of oocytes retrieved after stimulation and is **the best biomarker** for predicting poor and excessive ovarian response .
 - ✓ AMH <0.5 ng/mL predicts reduced ovarian reserve with < 3 follicles in an IVF cycle.
 - ✓ AMH <1.0 ng/mL predicts baseline ovarian reserve with a likelihood of limited eggs at retrieval.
 - ✓ AMH >1.0 ng/mL but < 3.5 ng/mL suggests a good response to stimulation.
 - ✓ AMH >3.5 ng/mL predicts a vigorous response to ovarian stimulation and caution should be exercised in order to avoid OHSS .
- Unlike the day 3 FSH, AMH can be **measured anytime** during the menstrual cycle and typically demonstrates minimal intercycle and intracycle variability since the growth of small preantral follicles that express it is continuous, not cyclical.



Assessment of fallopian tube patency

- We perform **HSG as the first-line test** for evaluation of tubal patency because of therapeutic, as well as diagnostic, benefits .
- HyCoSy is a reasonable alternative; the choice of test is determined by availability.
- When the diagnosis is in doubt, more invasive tests can be used to confirm the diagnosis and provide an opportunity for concurrent therapeutic intervention.
- These tests include laparoscopy with chromotubation and fluoroscopic/hysteroscopic selective tubal cannulation.



Hysterosalpingogram

- HSG is the standard of care to look for tubal occlusion in all patients , unless laparoscopy is planned .
- HSG is not useful for detecting peritubal adhesions or endometriosis .
- We perform diagnostic laparoscopy and chromotubation in women suspected of having endometriosis or pelvic adhesions related to a previous pelvic infection or surgery. Ablation of implants and lysis of adhesions, when indicated, can be performed at the same procedure.



- HSG appeared to have very **high specificity and sensitivity for diagnosing distal tubal occlusion** or major distal tubal adhesions, but much lower specificity for diagnosing proximal tubal occlusion .
- Proximal tubal occlusion on HSG often represents testing artifact due to tubal spasm or poor catheter positioning leading to unilateral tubal perfusion.



- Given these deficiencies, findings of proximal tubal occlusion on HSG could be confirmed by a secondary test such as a repeat HSG, fluoroscopic or hysteroscopic selective tubal perfusion, or laparoscopic chromotubation if definitive diagnosis will influence further management.
- Diagnostic HSG also appears to have **therapeutic effects**. A systematic review found that pregnancy rates were significantly higher in subfertile women who underwent tubal flushing with ***oil soluble media*** than in those who did not undergo HSG , and that pregnancy rates were similar whether oil or water soluble media were used .



Hysterosalpingo-contrast sonography(HyCoSy)

- Uses ultrasound to view the uterus, tubes, and adnexa before and after transcervical injection of echogenic contrast media (either microbubble contrast or agitated saline).
- It is a safe, well tolerated, quick and easy method for obtaining information on tubal status, the uterine cavity, the ovaries, and the myometrium using conventional ultrasound.
- In a systematic review of studies that compared **HyCoSy with HSG** for diagnosis of tubal occlusion in subfertile women, both tests had high diagnostic accuracy compared with laparoscopy (reference standard), with no significant difference between them.



Assessment of the uterine cavity

- Modalities to assess the uterine cavity include SIS , 3-D sonography, HSG , and hysteroscopy.
- SIS is the preferred imaging modality because:
 - ✓ it provides information about the endometrial cavity, myometrium, and adnexa.
 - ✓ is much better than routine ultrasonography for diagnosis of intrauterine adhesions, polyps, and congenital uterine anomalies and performs similarly to hysteroscopy at detecting intrauterine pathology .
- A variant of sonohysterography, HyCoSy, is a simple, time-efficient, and effective method to evaluate tubal patency, the uterine cavity, and the myometrium with one test .



- For women suspected of having a **uterine septum** on HSG, 3-D ultrasound or MRI can distinguish between a uterine septum and a bicornuate uterus.
- **Hysteroscopy** is the definitive method for evaluation of abnormalities of the endometrial cavity and also offers the opportunity for treatment at the time of diagnosis when performed in the operating room.
- Limitations of hysteroscopy include lack of information about the myometrium, fallopian tubes, and adnexal structures .



- If the endometrial cavity is assessed by another modality, routine use of hysteroscopy may not be necessary.
- We perform HSG or HyCoSy in infertile patients requiring assessment of tubal patency and uterine cavity evaluation.
- In women requiring only uterine cavity evaluation and no information on tubal status (eg, patients going directly to IVF for severe male factor), we perform either SIS or flexible hysteroscopy in the office to assess the uterine cavity.



ROLE OF LAPAROSCOPY

- The role of laparoscopy in the evaluation of infertility is controversial.
- Findings at laparoscopy usually **do not alter** the initial treatment of the infertile couple when:
 - ✓ the initial infertility evaluation is normal ,
 - ✓ when it shows severe male factor infertility
- Laparoscopy may be indicated in women in whom endometriosis or pelvic adhesions/tubal disease is suspected based on physical examination, HSG, or history .
- When we perform laparoscopy, we also perform chromotubation to assess tubal patency and hysteroscopy to evaluate the uterine cavity.
- For this reason, if laparoscopy is planned, then HSG can be omitted .



- Women with infertility but no endometriosis symptoms or prior surgical exploration undergo a **complete infertility evaluation, as do their partners.**
- Couples with a normal infertility evaluation (**unexplained** infertility) typically undergo a trial of **COH + / - IUI** , and many will conceive without further intervention.
- No randomized trials have assessed the cost-effectiveness and timing of diagnostic laparoscopy prior to ovulation induction in couples with unexplained infertility.
- Couples with **tubal or male** factor infertility are typically offered **IVF** as one of their treatment options and bypass laparoscopy.



TESTS OF LIMITED CLINICAL UTILITY

- In agreement with other experts, we do not recommend :
 - ✓ **Postcoital test** (intrauterine insemination and IVF, bypass the cervix, so improving cervical factors becomes irrelevant.
 - ✓ **Endometrial biopsy** (unless endometrial pathology is strongly suspected) .
 - ❖ Although endometrial receptivity during the implantation window is crucial for achieving pregnancy, histological assessment of endometrial response has a poor correlation with fertility .



- ✓ **Basal body temperature** records (interpretation of the charts can be difficult and subject to wide interobserver variation)
- ✓ **Mycoplasma & Ureaplasma cultures** (there is minimal evidence for a role of these organisms in female infertility)
- ✓ **Testing for antibodies** (Routine testing for antiphospholipid, antisperm, antinuclear, and antithyroid antibodies is not supported by existing data)
- ✓ **Karyotype** (We suggest karyotyping for :
 - ✓ women with POI ,
 - ✓ family history of early ovarian insufficiency (prior to age 40)
 - ✓ both partners if there have been recurrent pregnancy losses.)



Treatments



General principles of management of infertile couples

Involve both partners in the evaluation and management of infertility

Recommend lifestyle modifications to enhance fertility

Couple - Smoking cessation and reduce exposure to potential environmental toxins

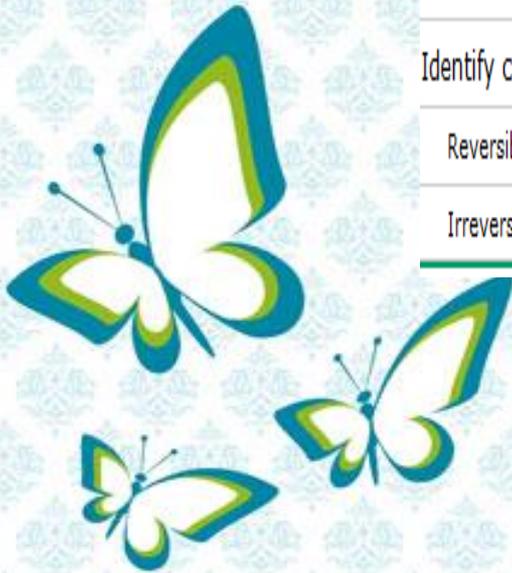
Women - Abstinence from alcohol, reduction of excessive caffeine intake, weight modulation to achieve target body mass index (20-25 kg/m²)

Perform infertility evaluation according to established guidelines

Identify causes of infertility

Reversible causes - Implement medical or surgical therapy to correct the etiology of infertility

Irreversible causes - Utilize assisted reproductive technologies, gamete donation, gestational carrier, adoption to overcome the etiology of infertility



CONTRAINDICATIONS

- The only absolute contraindications to infertility therapy are:
 - ✓ contraindication to pregnancy ,
 - ✓ contraindication to use of the drugs or surgeries used to enhance fertility.
- The ethics of restricting infertility therapy for other reasons, such as parental child-rearing ability, severe obesity, lifestyle issues (tobacco smoking, alcohol consumption), are controversial and beyond the scope of this review .



- Oligoovulation unrelated to ovarian failure can usually be treated successfully with ovulation induction;

- These women achieve fecundability nearly equivalent to that of normal couples (15 to 25 % probability of achieving a pregnancy in one menstrual cycle).

- However, normal fecundability is achieved at the expense of an increased risk of multiple pregnancy.



- The method of ovulation induction selected should be based upon the underlying cause of anovulation and the efficacy, costs, risks, and potential complications as they apply to the individual woman.
- Options include:
 - ✓ Weight modulation
 - ✓ Clomiphene citrate
 - ✓ Aromatase inhibitors
 - ✓ Gonadotropin therapy
 - ✓ Metformin or other insulin-sensitizing agents
 - ✓ Laparoscopic ovarian diathermy
 - ✓ Bromocriptine or other dopamine agonist (only in cases of hyper PRL + anovulation)
 - ✓ Assisted reproductive technology
- ***Most of these approaches are effective for WHO class 2 patients.***



- **WHO class 1** patients respond best to therapy involving lifestyle modification or gonadotropins.
- Some **WHO class 3** patients respond to gonadotropin therapy and IVF, but those who fail require oocyte donation.



TUBAL FACTOR INFERTILITY AND ADHESIONS

- For patients with **access to in IVF services**, IVF is first-line treatment for tubal factor infertility due to bilateral tubal obstruction.
- For women who **cannot access or decline IVF**, we offer surgical reconstruction to young patients with bilateral distal or proximal tubal obstruction.
- If surgery is successful, this approach has the advantages that additional treatment is not required for each attempt at conception, and it allows natural conception.



- For **older women** or women with **severe tubal disease** :

- ✓ bilateral hydrosalpinx,
- ✓ both proximal and distal occlusion,
- ✓ extensive adhesions,

we recommend **IVF** as the initial approach because tubal surgery is unlikely to be successful in these patients.

- Hydrosalpinges should be removed prior to IVF to optimize outcomes.



- **Unilateral proximal** tubal occlusion can be treated medically initially with COH .
- A case-controlled study found that **COH + IUI** in women with **unilateral proximal** tubal occlusion resulted in pregnancy rates statistically similar to those in patients with unexplained infertility, while patients with unilateral mid-distal or distal tubal occlusion had significantly lower pregnancy rates .



Procedures for improving tubal patency

- Surgery for the treatment of tubal factor infertility is **most successful** in women with **distal** tubal obstruction.
- Reconstructive surgery for **bilateral proximal** tubal occlusion is not very effective, and the risk of subsequent ectopic pregnancy is high, therefore, **IVF** is preferable, if available.



- For women with **unilateral proximal** tubal obstruction, at least one study reported similar pregnancy rates for women undergoing **COH-IUI** compared with women with bilaterally patent tubes and unexplained infertility also undergoing COH-IUI .



- Thus, for women with unilateral tubal occlusion for whom IVF is not an option, COH-IUI appears to be a reasonable alternative

UTERINE FACTOR INFERTILITY

- The finding of a uterine abnormality is not an indication for surgical intervention because *there is no uterine abnormality that is always associated with poor reproductive performance* .
- However, when a submucous fibroid, endometrial polyp, septate uterus, or uterine synechiae are discovered in the setting of **failure to conceive** or **recurrent pregnancy loss**, surgical correction should be considered since there may be a causal association.



Fibroids (leiomyoma)

- The relationship between fibroids and infertility is **controversial** and removal of fibroids is not clearly associated with improved fertility treatment outcomes .
- Couples should complete a **full infertility evaluation** before addressing the role of fibroids in their infertility.
- In general, the best candidates for myomectomy are women with a **submucosal** fibroid or an **intramural** fibroid that deforms the uterine cavity.



Synechiae, septa, congenital anomalies

- Intrauterine **synechiae** and **septa** may be uterine causes of infertility (particularly recurrent pregnancy loss) that may be surgically correctable by hysteroscopic resection.
- Two retrospective series showed a marked reduction in pregnancy loss after resection of a uterine septum or lysis of adhesions .
- *Women with severe irreparable uterine defects may require a gestational carrier.*



Endometrial polyps

- **Polypectomy** can improve fertility in **subfertile** women with **asymptomatic** endometrial polyps.
- In a trial that randomly assigned subfertile women with an endometrial polyp to hysteroscopic polypectomy before IUI or IUI alone found removal of the polyp significantly improved the pregnancy rate (pregnancy rate 63 % versus 28 %) .
- *We remove endometrial polyps in infertile women, even in the absence of abnormal bleeding.*



CERVICAL FACTOR INFERTILITY

- Cervical factor infertility is best treated by **IUI** to bypass cervical factors.
- **IVF** is the next option for patients with cervical factor infertility who fail to conceive with IUI.
- There is no strong evidence to support IUI in the absence of ovulation induction agents.



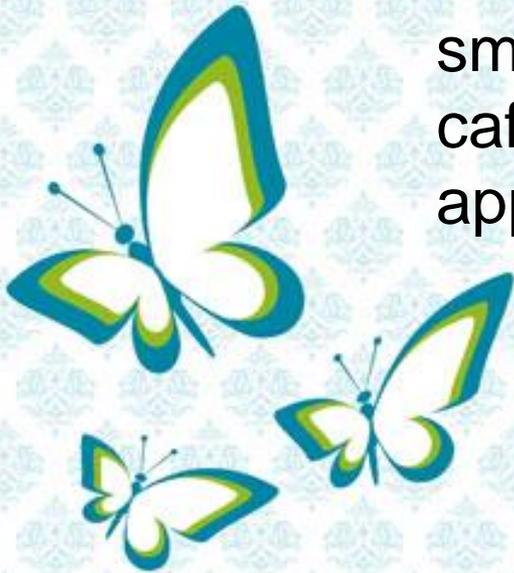
UNEXPLAINED INFERTILITY

- Couples with unexplained infertility have no identifiable etiology of their infertility after comprehensive evaluation; therefore, **treatment strategies are empiric.**
- Therapy with **clomiphene or letrozole + IUI** may be employed as initial treatment due to the low cost and low risk of side effects.
- If the patient does not conceive, **gonadotropin + IUI** or **ART** may be employed.



SUMMARY AND RECOMMENDATIONS

- Once the cause of infertility is identified, therapy is aimed at correcting reversible etiologies and overcoming irreversible factors.
- The couple is also counseled on lifestyle modifications to improve fertility, such as smoking cessation, reducing excessive caffeine and alcohol consumption, and appropriate frequency of coitus .



- The treatment of ovulatory dysfunction is based upon the underlying cause of anovulation (WHO class 1, 2, or 3 or hyperprolactinemia).
- **Oligoovulation** unrelated to ovarian failure can usually be treated successfully with **ovulation induction**.



- We offer **surgical** reconstruction to **young** patients with **bilateral** proximal or distal tubal obstruction and **limited** access to IVF , with counseling on the success rates of different methods of repair and on the high risk of EP .
- **IVF** is preferable to surgery in women with **severe** tubal disease (bilateral hydrosalpinx, both proximal and distal occlusion, extensive adhesions) and for **older** women, given the proven success of IVF in these patients.

Hydrosalpinges should be removed prior to IVF to optimize outcomes.



- Treatment of **subfertility** in women with **endometriosis** is generally approached by identifying and treating reversible causes of infertility followed by a sequential series of steps:
 - ✓ surgical resection of endometriosis,
 - ✓ ovulation induction plus IUI,
 - ✓ ART



- **Surgical** treatment of submucous fibroids, endometrial polyps, septate uterus, or uterine synechiae in the setting of failure to conceive or recurrent pregnancy loss appears to improve ongoing pregnancy rates.
- **Cervical** factor infertility is best treated by bypassing abnormal cervical factors using **IUI+ COH** .



Thanks all with best wishes

