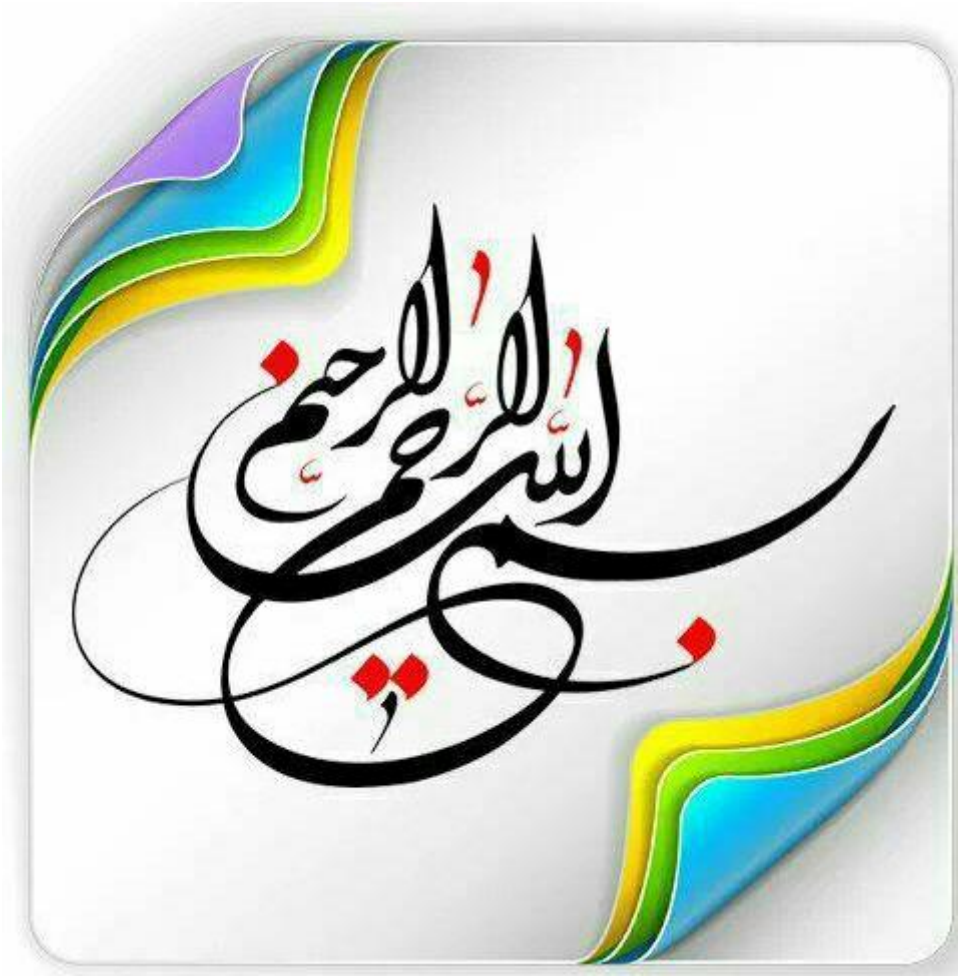
بسم الله الرحمن الرحيم

Etiologies of female infertility

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Etiologies of female infertility

In a World Health Organization (WHO) study of 8500 infertile couples:

female factor infertility :37 percent

male factor infertility : 8 percent

male and female factor infertility: 35percent

The remaining couples had unexplained

Infertility.

Most common identifiable female factors

Ovulatory disorders (25 percent)

Endometriosis (15 percent)

Pelvic adhesions (12 percent)

Tubal blockage (11 percent)

Other tubal abnormalities (11 percent)

Hyperprolactinemia (7 percent)

Ovulatory disorders

oligoovulation or anovulation results in infertility because an oocyte is not available every month for fertilization.

The World Health Organization has classified anovulation into three main groups, and recognizes hyperprolactinemia as additional etiology.

Oocyte aging

Age is an important factor affecting a woman's fertility .The decrease in fecundability with aging is likely due to a decline in both the

quantity and quality of the oocytes.

ovary reaches its apex of 6 to 7 million follicles in the mid-gestation female fetus, followed by a steady attrition from 1 to 2 million

follicles at birth to 300,000 follicles at the onset of puberty.

The rate of follicle loss accelerates after the woman reaches her mid-thirties .

Other insults to the ovary such as cigarette smoking, radiation, chemotherapy, and autoimmune disease also accelerate

follicular loss .Women with a depleted ovarian follicle pool may continue to ovulate regularly, but have infertility due to the poor quality of oocytes remaining in the terminal follicular pool

FALLOPIAN TUBE ABNORMALITIES/PELVIC ADHESIONS

Tubal disease and pelvic adhesions prevent normal transport of the oocyte and sperm through the fallopian tube.

The primary cause of tubal factor infertility is:

pelvic inflammatory disease

severe endometriosis

adhesions from previous surgery

nontubal infection (appendicitis, inflammatory bowel disease)

pelvic tuberculosis

salpingitis isthmica nodosa

Women with distal tubal obstruction may develop hydrosalpinges, which decrease the success rate of in vitro fertilization (IVF).

obstruction to sperm migration

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

Uterine fibroids are common benign smooth muscle monoclonal tumors.

that fibroids with a submucosal or intracavitary component can lower pregnancy and implantation rates.

as shown by improved pregnancy rates following removal of such Lesions.

Uterine anomalies

Uterine abnormalities are thought to cause infertility by interfering with normal implantation. Müllerian anomalies are a significant cause of recurrent pregnancy loss (RPL), 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.

ENDOMETRIOSIS

Mechanisms which decrease fertility in women with endometriosis include :

anatomic distortion from pelvic adhesions

damage to ovarian tissue by endometrioma formation and surgical resection

production of substances such as cytokines and growth factors which impair the normal

processes of ovulation, fertilization, and implantation.

CERVICAL FACTORS

Normal midcycle cervical mucus facilitates the transport of sperm.

Congenital malformations and trauma to the cervix (including surgery) may result in

stenosis and inability of the cervix to produce normal mucus, thereby impairing fertility.

INHERITED THROMBOPHILIA

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 in vitro fertilization success .

neither screening for thrombophilias nor treating them is advised in cases of repeated infertility treatment failure.

IMMUNE FACTORS

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.

Women with untreated celiac disease may have an increased frequency of reproductive abnormalities, including infertility, miscarriage, and

intrauterine growth restriction.

GENETIC CAUSES

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

47, XXY (Klinefelter syndrome) in men.

infertility evaluation

An infertility evaluation is usually initiated after one year of regular unprotected intercourse in women under age 35 years and after six months of unprotected intercourse in women age 35 years and older

However, the evaluation may be initiated sooner in women with:

irregular menstrual cycles

Known risk factors for infertility:

such as endometriosis

a history of pelvic inflammatory disease

reproductive tract malformations.

INITIAL APPROACH

Both partners of an infertile couple should be evaluated for factors that could be impairing fertility.

The infertility specialist then uses this

information to counsel the couple about the possible etiologies of their infertility and to offer a treatment plan targeted to their specific needs.

It is important to remember that the couple may have multiple factors contributing to their infertility. therefore, a complete initial diagnostic evaluation should be performed to detect the most common causes of infertility.

The recognition, evaluation, and treatment of infertility are stressful for most couples . The clinician should not ignore the couple's emotional state, which may include depression, anger, anxiety, and marital discord.

History and physical examination

Findings on history and physical examination may suggest the cause of infertility and thus help focus the diagnostic evaluation.

The most important points in the history are:

Duration of infertility and results of previous evaluation and therapy

Menstrual history:

regular monthly cycles with molimina (breast tenderness, ovulatory pain, bloating) suggest that the patient is ovulatory, severe dysmenorrhea suggest endometriosis.

cycle length may also be a general indicator of ovarian reserve. short menstrual cycle length (21 to 27 days) was associated with reduced ovarian reserve, including lower anti-müllerian hormone levels and antral follicle counts, compared with normal (28 to 31 days) and long (32 to 35 days) cycle lengths.

Medical, surgical, and gynecologic history (including sexually transmitted infections, pelvic inflammatory disease) to look for conditions, procedures, or medications potentially associated with infertility.

symptoms of thyroid disease, galactorrhea, hirsutism, pelvic or abdominal pain, dysmenorrhea, or dyspareunia.

Young women who have undergone unilateral oophorectomy generally do not have reduced fertility since young women have many primordial follicles per ovary; however, prior unilateral oophorectomy may impact fertility in older women as they may develop diminished ovarian reserve sooner than women with two ovaries.

- Obstetric history
- Sexual history, including sexual dysfunction and frequency of coitus.
- Family history
- Personal and lifestyle history including age, occupation, exercise, stress, dieting/changes in weight, smoking, and alcohol use.

Physical examination

- body mass index (BMI)
- 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.
- short and stocky, with a squarely shaped chest, suggests Turner syndrome in patients with absent periods

- Tenderness or masses in the adnexae or posterior cul-de-sac are consistent with chronic pelvic inflammatory disease or endometriosis.
- Palpable tender nodules in the posterior cul-de-sac, uterosacral ligaments, or rectovaginal septum are additional signs of endometriosis.
- Vaginal/cervical structural abnormalities or discharge suggest the presence of a müllerian anomaly, infection, or cervical factor.
- Uterine enlargement, irregularity, or lack of mobility are signs of a uterine anomaly, leiomyoma, endometriosis, or pelvic adhesive disease.

Diagnostic tests

- Semen analysis to detect male factor infertility.
- Documentation of normal ovulatory function. Women with regular menses with molimina are almost always ovulatory.
- A test to rule out tubal occlusion and assess the uterine cavity. We usually perform a hysterosalpingogram (HSG), or hysterosalpingo-contrast sonography
- laparoscopy with chromotubation
- A test or tests of ovarian reserve such as:
- cycle day 3 follicle-stimulating hormone (FSH) and estradiol
- clomiphene citrate challenge test
- anti-müllerian hormone
- antral follicle count.

Assessment of ovulatory function

Assessment of ovulatory function is a key component of the evaluation of the female partner since ovulatory dysfunction is a common cause of infertility.

- Women who have regular menses approximately every 28 days with molimina symptoms prior to menses (breast tenderness, bloating, fatigue, etc.) are most likely ovulatory.
- In women who do not describe their cycles as such, laboratory assessment of ovulation should be performed.
- mid-luteal phase serum progesterone level, which should be obtained approximately one week before the expected menses. For a typical 28-day cycle, the test
- would be obtained on day 21. A progesterone level >3 ng/mL is evidence of recent ovulation.

Other methods of determining ovulation, such as daily ultrasounds to follow the development and ultimately the disappearance of a follicle (the most accurate

method of documenting ovulation)and endometrial biopsy to document secretory changes in the endometrium are too expensive or invasive .

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 polycystic ovary syndrome (PCOS).

An alternative is to have the patient use an over-the-counter urinary ovulation prediction kit. These kits detect luteinizing hormone (LH) and are highly effective for predicting the timing that reliably indicates ovulation. Home kits have a 5 to 10 percent false positive and false negative rate. Therefore, serum confirmation can be useful in patients who are unable to detect a urinary LH surge.

Basal body temperature

are the least expensive method for detecting ovulation.

Progesterone released from the corpus luteum at the time of ovulation has potent effects on the hypothalamus, one of which is to increase body temperature.

The woman takes her temperature by putting the:

thermometer under her tongue every morning while she is still in the basal state and records the temperature on a chart.

an approximately 0.5ºF rise in body temperature can be detected

in the luteal phase of the menstrual cycle compared with the follicular phase. In a normal cycle, the temperature rise begins one or two days after the LH surge and persists for at 10 days.

Assessment of ovarian reserve

Diminished ovarian reserve can refer to diminished oocyte quality, oocyte quantity, or reproductive potential.

identification of diminished ovarian reserve is an increasingly important component of the initial infertility evaluation.

coordination of tests provides the best assessment.

We test ovarian reserve with an AMH level and a day 3 FSH and estradiol levels.

Other tests such as:

the clomiphene citrate challenge test (CCCT)
antral follicle count

are utilized by some specialists and in special circumstances.

Day 3 FSH and CCCT

Both the day 3 FSH level (where day 1 is the first day of full menstrual flow) and the CCCTare widely used for screening ovarian reserve.

The CCCT involves oral administration of 100 mg clomiphene citrate on cycle days 5 through 9 with measurement of day 3 and day 10 FSH levels and day 3 estradiol level.

the day 3 FSH less than 10 milliinternational

units/mL suggestive of adequate ovarian reserve, and levels of 10 to 15 milli-international units/mL borderline.

day 3 estradiol level <80 pg/mL suggestive of adequate ovarian reserve.

day 3 estradiol levels >80 pg/mL resulted in higher cycle cancellation rates and lower pregnancy rates, and estradiol levels >100 pg/mL

were associated with a 0 percent pregnancy rate .

Anti-müllerian hormone

AMH is expressed by the small (<8 mm) preantral and early antral follicles.
Can be measuured any time during the menstrual cycle.

reflects the size of the primordial follicle pool, and may be the best biochemical marker of ovarian function .
AMH levels gradually decline as the primordial follicle pool declines with age
AMH is undetectable at menopause.
In patients planning IVF, AMH level is the best biomarker for predicting poor and excessive ovarian response.

AMH <0.5 ng/mL predicts reduced ovarian reserve with less than 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 ovarian hyperstimulation syndrome.

Assessment of fallopian tube patency

HSG as the first-line test for evaluation of tubal patency because of therapeutic, as well as diagnostic benefits.

HyCoSy is a reasonable alternative.

When the diagnosis is in doubt, more invasive tests can be used to confirm the diagnosis.

These tests include:

laparoscopy with chromotubation fluoroscopic/hysteroscopic selective tubal cannulation.

Hysterosalpingogram

- HSG is the standard of care to look for tubal occlusion in all patients.
- Water or lipid-soluble contrast media is used to fill the uterus and fallopian tubes.
- HSG also provides information about the uterine cavity.
- HSG is not useful for detecting peritubal adhesions or endometriosis.

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 due to tubal spasm or poor catheter positioning leading to unilateral tubal perfusion.

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.

pregnancy rates were significantly higher in

subfertile women who underwent tubal flushing with oil soluble media than in those who did not undergo HSG.

Hysterosalpingo-contrast sonography

Hysterosalpingo-contrast sonography (HyCoSy) uses ultrasound to view the uterus, tubes, and adnexa before and after transcervical injection of echogenic contrast media.

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.

Assessment of the uterine cavity

Modalities to assess the uterine cavity :

saline infusion sonohysterography

three-dimensional sonography

hysterosalpingography (HSG)

hysteroscopy.

Saline infusion sonohysterography is the preferred imaging modality to assess the uterine cavity because it provides information about the endometrial cavity, myometrium, and adnexa.

HSG is typically performed to assess tubal patency, HSG can also identify developmental or acquired abnormalities of the uterine cavity that negatively impact fertility, such as submucous fibroids, a T-shaped cavity ,polyps, synechiae, and congenital müllerian anomalies.

For women suspected of having a uterine septum :

three-dimensional ultrasound
magnetic resonance imaging.

Abnormalities found on HSG generally require further evaluation :
three-dimensional sonography
sonohysterography
magnetic resonance imaging
hysteroscopy, or laparoscopy

Hysteroscopy is the definitive method for evaluation of abnormalities of the endometrial cavity.

Limitations of hysteroscopy include lack of information about the myometrium, fallopian tubes, and adnexal structures.

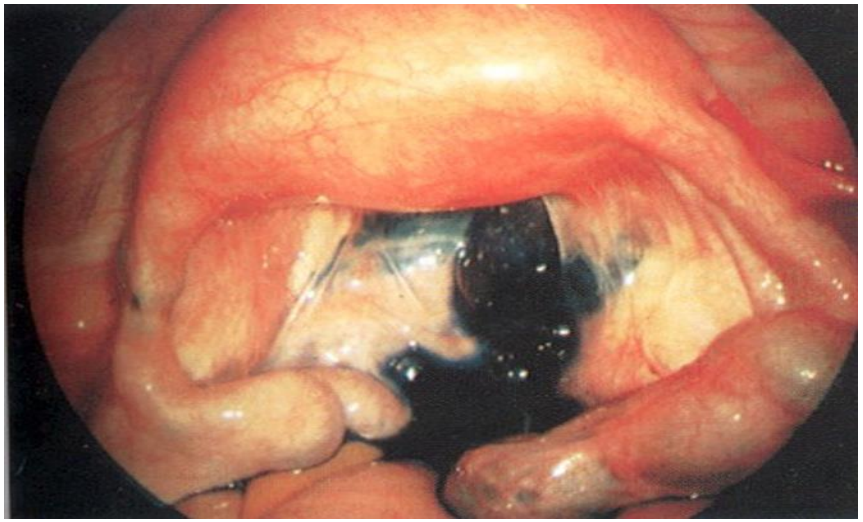
In women requiring only uterinecavity evaluation we perform either:

saline infusion sonohysterography

flexible hysteroscopy in the office

LAPAROSCOPY

Laparoscopy may be indicated in women in whom endometriosis or pelvic adhesions/tubal disease is suspected based on physical examination, HSG, or history.



Karyotype

There is a general consensus to counsel and offer to karyotype the male partner if there is severe oligospermia, as these men are at higher risk of karyotypic abnormalities.

Separate testing for Y chromosome microdeletions may also be offered.

We suggest karyotyping women :

with premature ovarian insufficiency

or a family history of early ovarian insufficiency (prior to age 40)

and both partners if there have been recurrent pregnancy losses.

karyotyping is not indicated as part of the initial evaluation because of the low incidence of abnormalities in women with unexplained infertility, endometriosis, or tubal factor infertility .

Treatement

Once the cause of infertility is identified, therapy aimed at correcting reversible etiologies and overcoming irreversible factors can be implemented.

lifestyle modifications to improve fertility, such as smoking cessation, reducing excessive caffeine and alcohol consumption.

The patient should be involved in fertility treatment choices. These choices involve four major factors:

effectiveness (live birth rate), burden of treatment (frequency of injections and office visits), safety (risk of ovarian hyperstimulation and multiple gestation), and financial costs.

OVULATORY DISORDERS

WHO class 1 – Hypogonadotropic hypogonadal anovulation is the least common, occurring in 5 to 10 percent of cases. Examples of women in this category:

are women with hypothalamic amenorrhea from functional etiologies such as excessive exercise or low body weight.

WHO class 2 – Normogonadotropic normoestrogenic anovulation is the most common, accounting for 70 to 85 percent of cases. Women with polycystic ovary syndrome usually fall into this category.

WHO class 3 – Hypergonadotropic hypoestrogenic anovulation occurs in 10 to 30 percent. Women with primary gonadal failure (previously called premature ovarian failure) or gonadal dysgenesis, comprise the majority of these cases.

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 percent probability of achieving a pregnancy in one menstrual cycle) .

The method of ovulation induction selected should be based upon the underlying cause of anovulation and the efficacy, costs, risks, and potential complication sassociated with each method as they apply to the individual woman.

Options include:

- Weight modulation
- Clomiphene citrate
- Aromatase inhibitors
- Gonadotropin therapy
- Metformin
- Laparoscopic ovarian diathermy
- Bromocriptine or other dopamine agonist
- 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 orgonadotropins.

Some WHO class 3 patients respond to gonadotropin therapy and in vitro fertilization (IVF), but those who fail require oocyte donation.

Weight modulation

Women who are far above or below ideal body weight are prone to ovulatory dysfunction and subfertility .Weight modulation in these women can enhance fertility.

High body weight : Women with body mass index (BMI) greater than 27 kg/m and anovulatory infertility are advised to lose weight.

For obese women with polycystic ovarian syndrome (PCOS), the loss of just 5 to 10 percent of body weight is sufficient to restore ovulation in 55 to 100 percent of these women within six months .

Weight loss should be a first-line treatment for obese anovulatory women.

Low body weight Anovulatory women with low BMI (less than 17 kg/m) with eating disorders, or strenuous exercise regimens, may develop:

hypogonadotropic hypogonadism and/or hypothalamic amenorrhea (WHO class 1) .

Psychogenic stress may also disrupt the gonadotropin releasing hormone (GnRH) pulse generator and impair ovarian function

as a result of reduced pituitary gonadotropin secretion .

Such women should be advised:

to gain weight

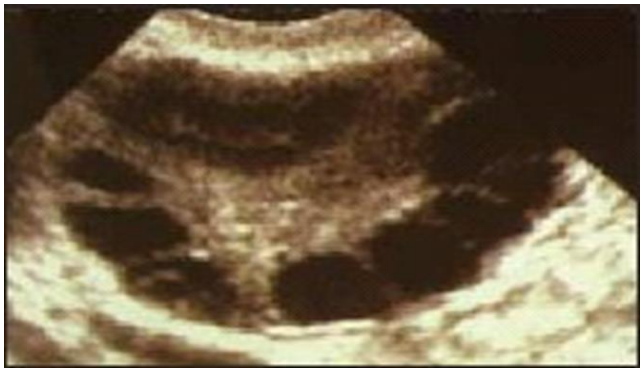
modify diet

reduce exercise.

Ovulation induction agents

Clomiphene citrate is a selective estrogen receptor modulator (SERM) with both estrogen antagonist and agonist effects that increase gonadotropin release.

It is an effective method of inducing ovulation and improving fertility of oligoovulatory women in WHO class 2.



Aromatase : Anovulatory WHO 2 patients who have a poor outcome with clomiphene (no ovulation or thin endometrium) may have a better response with aromatase inhibitors.

Advantages of these agents over clomiphene include:

(1) production of fewer follicles and lower estradiol levels, thereby decreasing the risk of multiple gestation.

(2) shorter half-life (50 hours versus 5 days), resulting in reduced antiestrogen effects on the endometrium and cervical mucus.

In patients with polycystic ovarian syndrome, a multicenter randomized double-blind trial showed that letrozole was superior to clomiphene in inducing ovulation and live birth.

The FDA has not approved aromatase inhibitors for treatment of infertility.

Metformin : Insulin resistance is commonly observed in women with PCOS. Correction of hyperinsulinemia with metformin has a beneficial effect in anovulatory

women with PCOS because this leads to an increase in menstrual cyclicity and enhanced spontaneous ovulation. However, live birth rates are not as high as those

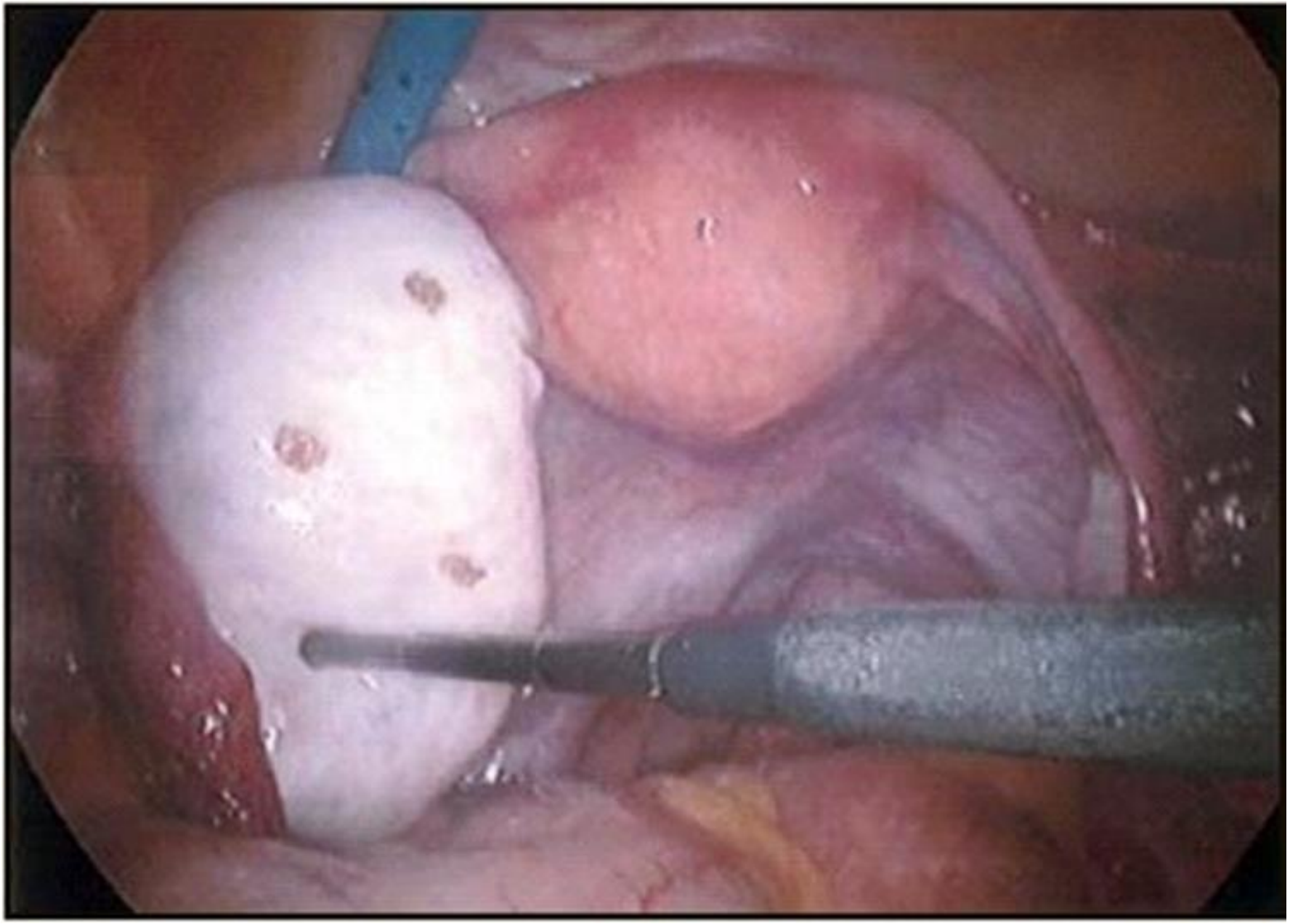
achieved with clomiphene.

However, the addition of metformin in this setting may help facilitate weight loss and ovulation. In addition, metformin may provide additional metabolic effects that are beneficial for pregnancy.

Laparoscopic surgery : Laparoscopic ovarian drilling by diathermy or laser is a surgical treatment to induce ovulation in anovulatory PCOS patients.

However, the rate of multiple pregnancy was considerably lower in women who conceived after ovarian drilling.

As laparoscopic ovarian diathermy is invasive and carries more risk for the patient than medical therapy, we reserve its use for patients who fail to conceive with alternative treatments and after other fertility factors have been thoroughly investigated and corrected.



Dopamine agonists : Dopamine agonists, such as bromocriptine, are the treatment of choice for women with hyperprolactinemic anovulation.

Assisted reproductive technologies:

Oligoovulatory women who do not conceive with other fertility treatments may be considered for IVF.

WHO class 3 patients :

women with premature ovarian failure may require oocyte donation by a known or anonymous donor who undergoes controlled ovarianhyperstimulation and oocyte retrieval.

TUBAL FACTOR INFERTILITY AND ADHESIONS

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 proxima ltubal obstruction.

For women with severe tubal disease (bilateral hydrosalpinx, both proximal and distal occlusion, extensive adhesions) and for older women, we recommend :

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

Unilateral proximal tubal occlusion:

can be treated medically initially with controlled ovarian hyperstimulation.

A retrospective case-controlled study found that

controlled ovarian hyperstimulation with intrauterine insemination (IUI) in women with unilateral proximal tubal occlusion resulted in pregnancy rates statistically

similar to those in patients with unexplained infertility (31 versus 43 percent), while patients with unilateral mid-distal or distal tubal occlusion had significantly

lower pregnancy rates (19 versus 43 percent).

Procedures for improving tubal patency

Surgery for the treatment of tubal factor infertility is most successful in women with distal tubal obstruction.

Fimbrioplasty, the lysis of fimbrial adhesions

or dilatation of fimbrial strictures, and neosalpingostomy, the creation of a new tubal opening in a distally occluded tube, may be performed via laparotomy or laparoscopy.

Reconstructive surgery for bilateral proximal tubal occlusion is not very effective, and the risk of subsequent ectopic pregnancy is

high (as high as 20 percent) .Therefore, IVF is preferable, if available.

In vitro fertilization
Advantages

- Better per-cycle success rate than other fertility treatments
- Less surgically invasive than tubal surgery
- Can overcome other subfertility factors, if present (male factor, cervical factor, decreased ovarian reserve)
- Site and extent of tubal damage are not important to outcome

Disadvantages:

- High per cycle cost and possible need for multiple cycles
- Need for IVF each time a pregnancy is desired
- Requires frequent injections and monitoring
- Increases risk of multiple gestation
- Increases risk of ovarian hyperstimulation syndrome
- Possibly slightly higher absolute risk of some adverse perinatal outcome than natural conception

- laparoscopic salpingectomy in women with hydrosalpinges improves the outcomes of IVF treatment compared with no surgical intervention .
- The improvement in pregnancy and live birth rates is likely due to the removal of a source of embryotoxic substances or fluid into the uterus disrupting implantation.

- It has been hypothesized that the surgical removal of hydrosalpinges might decrease blood supply to the ovaries and compromise ovarian reserve , but this has not been studied.
- In a meta-analysis of seven trials, proximal tubal occlusion and salpingectomy each resulted in increased rates of ongoing pregnancy following IVF in women with hydrosalpinges .
- Further investigation is required to assess whether alternative surgical treatments for hydrosalpinx removal (salpingostomy, tubal occlusion, needle drainage of hydrosalpinx at oocyte retrieval) are more effective than salpingectomy.

ENDOMETRIOSIS

Treatment of subfertility in women with endometriosis is approached by identifying and treating reversible causes of infertility followed by sequential application of various therapies:

surgical resection of endometriosis, ovulation induction plus intrauterine insemination, and assisted reproductive technologies.

We generally use this stepwise approach, except in the setting of multiple infertility factors (significant male factor component, decreased ovarian reserve, pelvic factors) because the presence of multiple factors has a large negative effect on conservative therapy.

For these cases, we would probably go straight to in vitro fertilization .

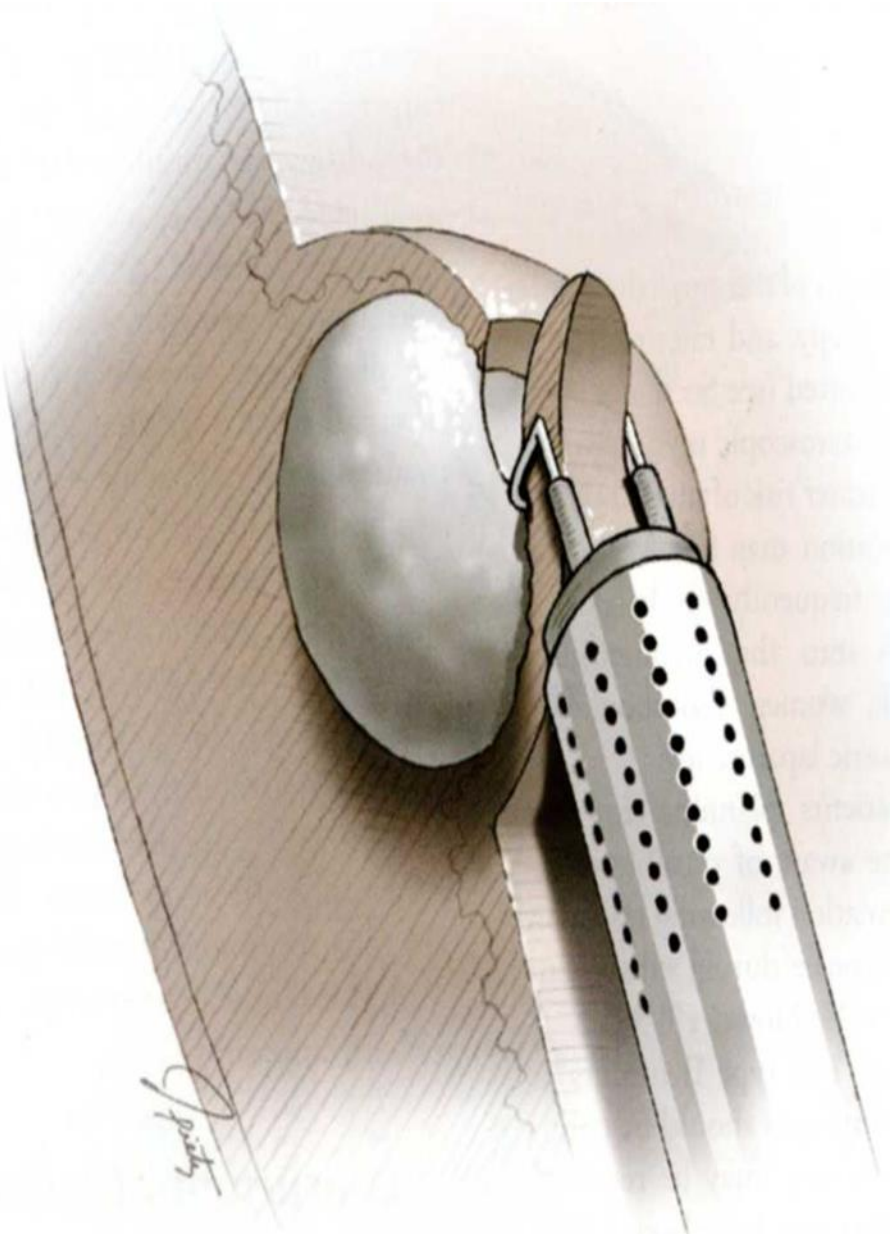
In addition, moving directly to in vitro fertilization in patients with high-stage endometriosis seems prudent.

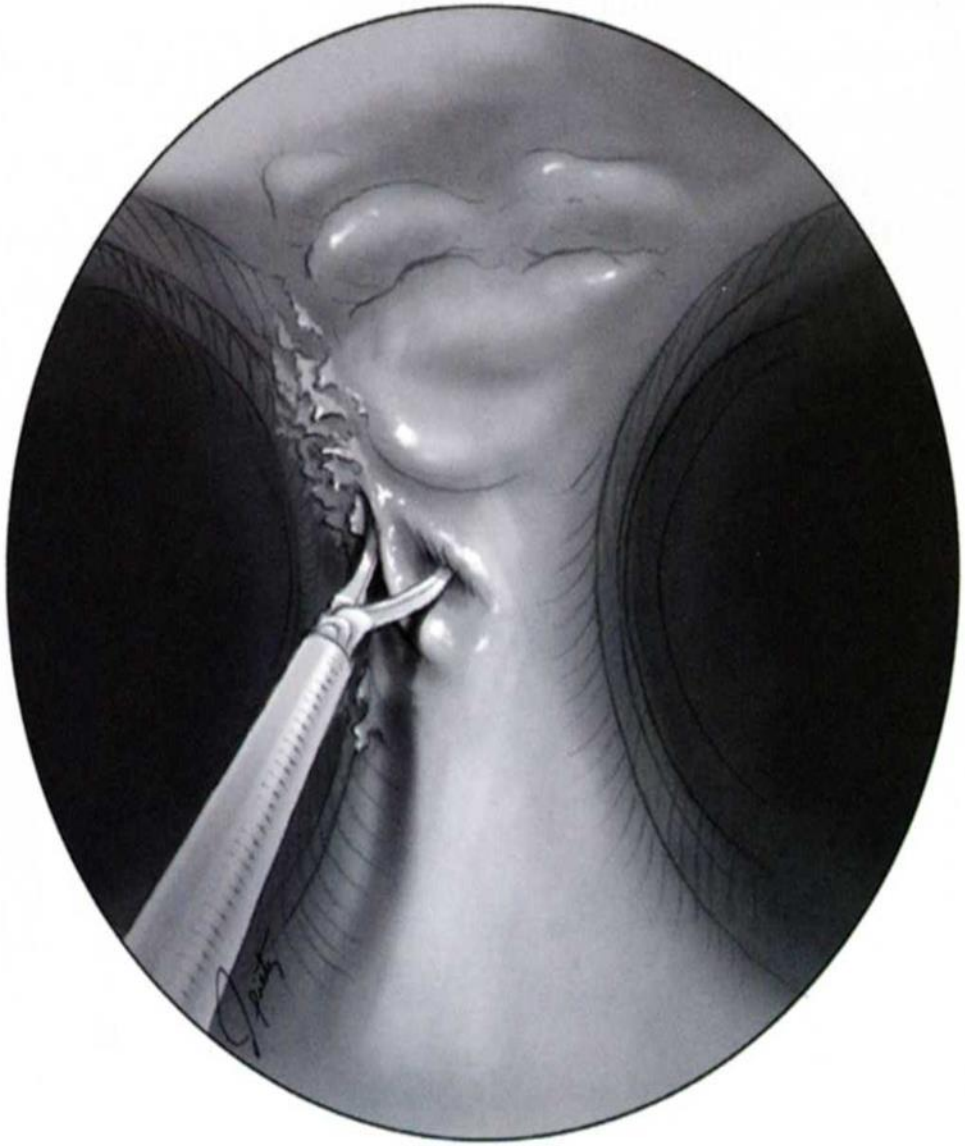
UTERINE FACTOR INFERTILITY

when a, endometrsubmucous fibroidial 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.

Women with severe irreparable uterine defects may require a gestational carrier.





Polypectomy can improve fertility in subfertile women with asymptomatic endometrial polyps.

This was illustrated in a trial that randomly

assigned subfertile women with an endometrial polyp to hysteroscopic polypectomy before intrauterine insemination (IUI) or IUI alone and found removal of the

polyp significantly improved the pregnancy rate (pregnancy rate 63 percent after polypectomy versus 28 percent with IUI alone) .Based on this trial, and other

data from observational studies, we remove endometrial polyps in infertile women, even in the absence of abnormal bleeding.

UNEXPLAINED INFERTILITY

Therapy with clomiphene with intrauterine insemination (IUI) may be employed as initial treatment due to the low cost and low risk of side effects.

If the patient does not conceive after clomiphene with IUI:

gonadotropin injections with IUI

assisted reproductive technologies