POOR OVARIAN RESERVE

Impaired Ovarian Reserve, Premature Ovarian Aging, Declining Ovarian Reserve, Poa

A condition of low fertility characterized by low numbers of remaining oocytes in the ovaries or possibly impaired oocyte development or recruitment.

Related Diagnoses:
Anovulation | Premature ovarian failure

About Poor ovarian reserve

Ovarian reserve is a term that is used to determine the capacity of the ovary to provide egg cells that are capable of fertilization resulting in a healthy and successful pregnancy. With advanced maternal age the number of egg cell that can be successfully recruited for a possible pregnancy declines, constituting a major factor in the inverse correlation between age and female fertility.

The primary theory being held to explain the poor ovarian reserve is the depletion of the ovarian pool of non-growing follicles, believed to be at its maximum in-utero and shrinking gradually towards menopause. Several mechanisms have been suggested to explain the decline in oocyte quantity and quality. These include possible differences in germ cell formation during fetal life, changes in the quality of the granulosa cells surrounding the oocyte as well as accumulated damage to the oocytes during childhood and reproductive life. However, the exact mechanism(s) are still mostly obscure.

Approximately 10% of women deviate from age-specific standards and, before reaching menopause, are assumed to suffer from premature ovarian aging (POA). The size of a woman’s initial follicle pool between birth and menarche is of great importance because it reflects the symbolic starting point of follicle
depletion. Published ovarian reserve models demonstrate that, due to genetic preprogramming, pools vary greatly in size.

The most important predictors of the ovarian response to hormonal stimulation are age, biochemical parameters (basal FSH levels in the early follicular phase, serum antimullerian hormone [AMH]), and morphological characteristics (antral follicular count [AFC] and ovarian volume).

Although ovarian reserve declines with age, it does not represent an optimal predictor of ovarian response. **Basal serum FSH (follicle stimulating hormone) concentrations begin to rise on average a decade or more before the menopause.** More recently it has been demonstrated that it is a good predictor only at very high threshold levels (>FSH 12 mIU/mL) predicting a very compromised ovarian reserve.

**AMH is produced from preantral follicles and small antral follicles** up to 7-8 mm. AMH provides a quantitative evaluation of the amount of follicles that cannot be assessed by AFC. For this reason AMH level has a very low inter- and intracycle variability remaining stable during menstrual cycles but some factors like smoking and current oral contraceptive pills can determine variability. A recent meta-analysis has confirmed AMH an excellent predictor of poor ovarian response to ovarian stimulation although the ideal test is the response of the ovaries to ovarian stimulation itself.

However, the same meta-analysis underlines that AMH and AFC, alone or in combination, did not improve the prediction of ongoing pregnancy rate, with the age of the woman being the most important factor related to live birth rates.

Poor ovarian reserve can be treated with hormonal stimulation. Predicting ovarian response before starting hormonal stimulation is the only way to administer an efficient and safe treatment.

Considering modern trends of maternity postponement and the increasing demand for assisted reproduction technologies (ART), the evaluation of functional ovarian reserve has arisen in an attempt to better advise interested couples, helping physicians in the inference of follicular response and success rates, and guiding the elaboration of individualized stimulation protocols, with a reduction of emotional and financial burdens of hard and stressful therapeutic processes. In this context, the identification of women with a lower reproductive potential is a great challenge for reproductive medicine specialists.

**Associated diseases**
Premature ovarian failure (POF)

Premature ovarian failure is defined as no menses for six months before the age of forty due to any cause. Often diagnosed by elevated gonadotropin (Follicle-stimulating hormone (FSH) and Luteinizing hormone (LH) levels. In some cases (more so in younger women) ovarian function and ovulation can spontaneously resume. With POF up to 50% of women may ovulate once in any given year and 5–10% may become pregnant. POF is often associated with autoimmune diseases.

Premature menopause

Premature menopause is a outdated synonym for premature ovarian failure. The term encompasses premature menopause due to any cause, including surgical removal of the ovaries for any reason. Early menopause and premature ovarian failure are no longer considered to be the same condition.

Complications

- infertility

Risk factors

In poor responders the mechanism of ovarian insufficiency is prematurely determined and not fully understood. Some causes of decrease in ovarian reserve have been identified: ovarian surgery especially in case of endometrioma, genetic defects, chemotherapy, radiotherapy, autoimmune disorders, single ovary, chronic smoking, and unexplained infertility. Moreover, new risk factors of low ovarian response have been proposed: diabetes mellitus Type I, transfusion-dependent B-thalassemia, and uterine artery embolization for the treatment of uterine leiomyoma.

Lastly, some data underlines the role of body mass index (BMI) in female reproduction: obese poor responders could have a lower pregnancy rate than nonobese poor responders.

Impact on fertility

One of the fundamental steps to reach the success is still related to the number of eggs obtained after hormonal stimulation by gonadotropins in
combination with GnRH analogues. In patients defined “poor responders,” the limited number of obtained eggs remains the main problem in optimizing the live birth rates. In fact, as a result of a lower number of oocytes retrieved, there are fewer embryos to select and transfer and subsequently these patients have lower pregnancy rates per transfer and lower cumulative pregnancy rates per started cycle compared with normal responders.

**Prevention**

Maternal diet which eliminates high fat/high sugar during pregnancy influences the later life reproductive potential of female offspring. The reproductive system appears to be exquisitely sensitive to early life influences. Maternal diet during pregnancy affects numerous parameters including follicular reserve.

**Symptoms**

- infertility

**Therapies**

**Self therapy**

Chinese medicine

Chinese medicine (CHM) has played a unique advantage to improve egg quality and ovarian response, enable a reduction in the dose of gonadotrophin, increase pregnancy rate, and reduce the incidence of ovarian hyperstimulatin syndrome (OHSS).

Chinese medicine also helps the patients undergo the in vitro fertilization. The mechanisms of adjuvant therapy with CHM in IVF patients may be as follows: (1) reduced ovarian blood flow resistance and increased ovarian perfusion, thus promoting the follicular development and improving the quality of oocyte, (2) improved the endometrial microcirculation and increased the blood flow of endometrium, promoted endometrial thickened, and improved endometrial receptivity and embryo implantation, leading to higher success rate of embryo implant.
**Conventional medicine**

**Pharmacotherapy**

There are several stimulation protocols, which can improve the outcome in poor responding patients. The final decision is always based on patient's doctor and patient itself.

The stimulation is primarily done with the gonadotropins. Gonadotropins are hormones, which stimulate the pituitary gland to produce follicle stimulating hormone. If there is an initial poor response, it often leads to an increase in dosage. Some studies have showed that there is a small benefit in this strategy. The number of follicles for growth varies every month and no increase in dosage will alter this number.

Fortunately, there is possibility to combine stimulating medication with anti-oestrogens and dehydroepiandrosterone. Anti-oestrogens (e.g. Clomiphene) are combined with FSH injections and this maximizes the ovarian response. The purpose is to mask the brain women’s own oestrogen levels, and the pituitary gland will produce more FSH and stimulate the ovary.

Dehydroepiandrosterone (DHEA) is a steroid hormone which is a precursor of testosterone and oestrogen and decreases with age. The benefit is that DHEA can be used as a supplementation of oestrogen which is necessary for follicle growth.

**Surgical therapy**

There is no surgical therapy for this condition.

**Assisted reproduction**

Natural or Mini-IVF (minimal stimulation in vitro fertilization protocol), but without the use of hCG to trigger ovulation, instead the GnRH agonist (a synthetic peptide that interacts with the gonadotropin-releasing hormone receptor to elicit its biologic response) in a diluted form is taken as a nasal spray to trigger ovulation. Human chorionic gonadotropin (hCG) has a long half-life and may stimulate (luteinize) small follicles prematurely and cause them to become cysts. Whereas nafarelin acetate in a nasal spray induces a short lived luteinizing
hormone surge that is high enough to induce ovulation in large follicles, but too short lived to adversely affect small follicles. This increases the likelihood of the small follicles and oocytes therein developing normally for upcoming cycles and also allows the woman to cycle without taking a break and consequently increases the probability of conception in poor ovarian reserve women and advanced reproductive aged women.

Oocyte donation followed by in vitro fertilization is the most successful method for producing pregnancy in perimenopausal women with no ovarian response. After stimulation of donor, the physician surgically extracts one or more eggs from the ovary, and unites them with sperm in a laboratory setting, with the intent of producing one or more embryos. The fertilized eggs (embryos) are cultivated under very stringent conditions and examined every day by the embryologist to evaluate their progress. The embryos are usually cultured for 3 to 5 days, before the best one(s) are selected to be put (transferred) in to the womb.

Find more about related issues

Diagnoses

Anovulation
Failure of the ovaries to release an oocyte over a period of time generally exceeding 3 months.
Learn more at: www.fertilitypedia.org/therapy/diag/anovulation

Premature ovarian failure
The loss of function of the ovaries before age 40.
Learn more at: www.fertilitypedia.org/therapy/diag/premature-ovarian-failure

Organs

Ovary
The ovum-producing organs of the internal female reproductive system
Learn more at: www.fertilitypedia.org/edu/organs/ovary

Reproductive cells
Oocyte
A female germ cell involved in reproduction.
Learn more at: www.fertilitypedia.org/edu/reproductive-cells/oocyte

Biological control

Anti-Müllerian hormone
A hormone, that provokes the regression of male fetal Müllerian ducts.
Learn more at: www.fertilitypedia.org/edu/biological-control/anti-mullerian-hormone

Follicle-stimulating hormone
FSH is a hormone secreted by the anterior pituitary gland. It regulates the development, growth, pubertal matur and reproductive functions of the body
Learn more at: www.fertilitypedia.org/edu/biological-control/follicle-stimulating-hormone

Risk factors

High level of FSH
FSH levels above what an expected levels for one’s age and is indicator of proper ovarian function.
Learn more at: www.fertilitypedia.org/therapy/rf/high-level-of-fsh

Low level of AMH
Low blood levels of AMH (anti-Müllerian hormone) which may indicate poor ovarian reserve.
Learn more at: www.fertilitypedia.org/therapy/rf/low-level-of-amh

Symptoms

Decreased level of AMH
Lower levels of Anti-Müllerian hormone according to the age.
Learn more at: www.fertilitypedia.org/edu/symptoms/decreased-level-of-amh

Increased level of FSH
A condition with high serum follicle–stimulating hormone (FSH) concentration.
Learn more at: www.fertilitypedia.org/edu/symptoms/increased-level-of-fsh

Therapies
**Egg donation**
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: [www.fertilitypedia.org/edu/therapies/egg-donation](http://www.fertilitypedia.org/edu/therapies/egg-donation)

**ICSI**
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: [www.fertilitypedia.org/edu/therapies/icsi](http://www.fertilitypedia.org/edu/therapies/icsi)

**Sperm donation**
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: [www.fertilitypedia.org/edu/therapies/sperm-donation](http://www.fertilitypedia.org/edu/therapies/sperm-donation)

**Standard IVF**
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: [www.fertilitypedia.org/edu/therapies/standard-ivf](http://www.fertilitypedia.org/edu/therapies/standard-ivf)

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