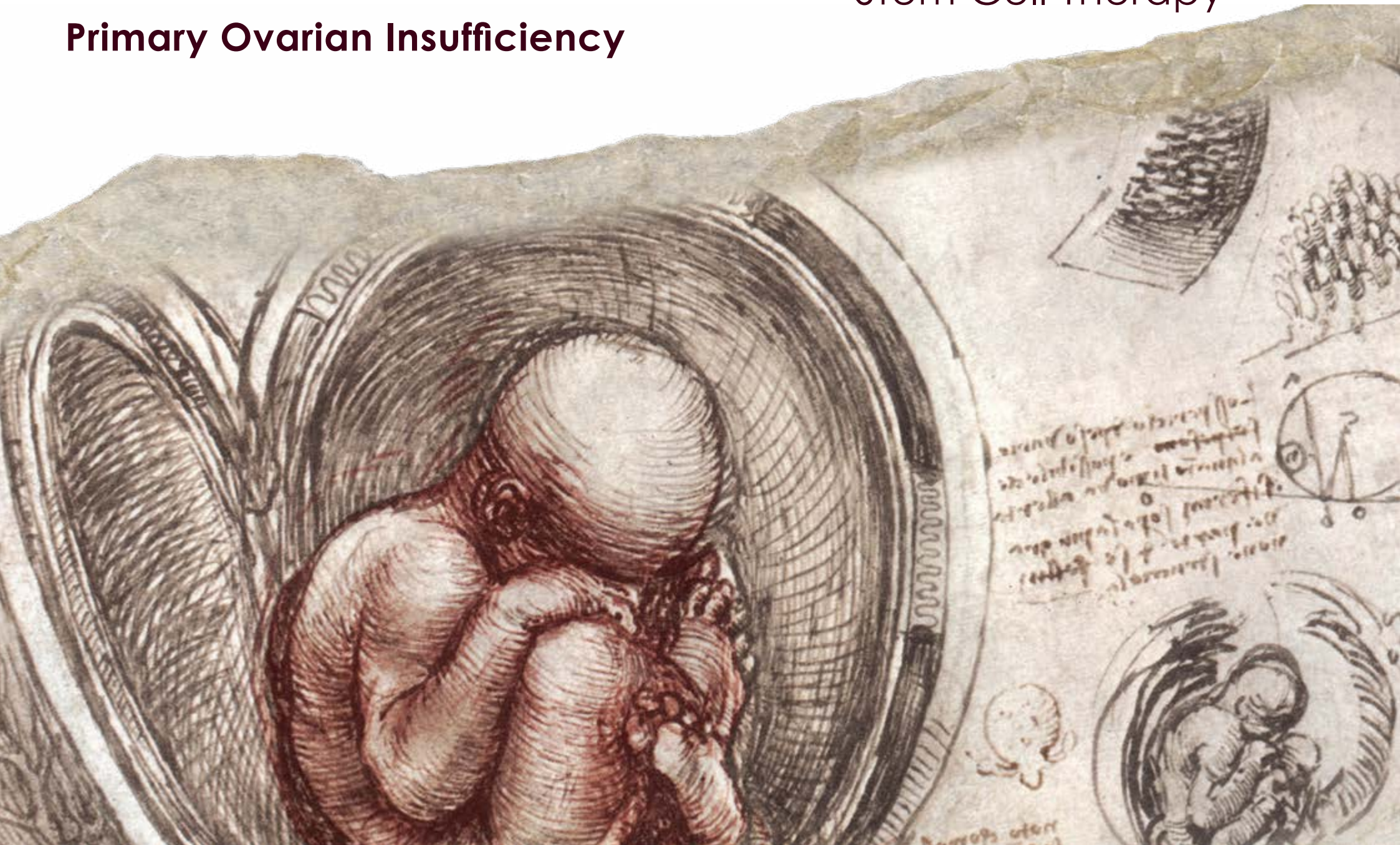
Early Menopause

Premature Ovarian Failure

Primary Ovarian Insufficiency

OVOSKILL

Stem Cell Therapy



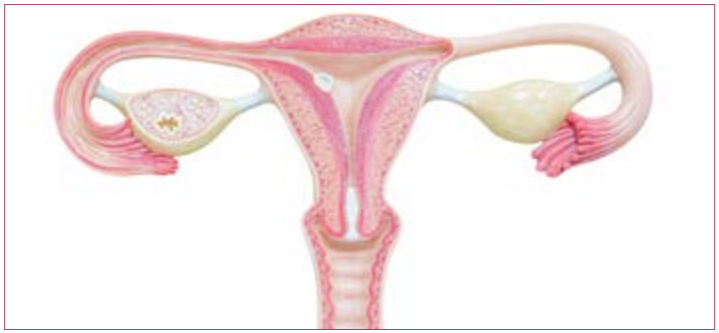
PREMATURE OVARIAN FAILURE

Ovaries usually produce hormones and eggs until the early fifties, when they stop working and most women enter menopause. However, in some cases women can enter early menopause because of **Premature Ovarian Failure** (POF), a common gynecological endocrine disease also known as primary ovarian insufficiency.

POF is characterized by the loss of ovarian function at age below 40 years. It represents the cause of 10-28% of cases of primary amenorrhea (that is, the failure of menses to occur by age 16) and of 4-18% of cases of secondary amenorrhea (the cessation of menses for 6 months or longer).

Its prevalence is 1/250 in women under 35 years and 1/100 in women under 40 years, and the trend in its incidence is increasing due to the effects of multiple factors, among which the wide use of chemotherapy plays a significant role. Most often, it is a non-reversible pathology leading to **infertility** and severely affecting women both physically and mentally.

COMPLICATIONS	SYMPTOMS
osteoporosis	amenorrhoea
cardiovascular diseases	estrogen deficiency
hot flushes, night sweats	elevated gonadotropin
vaginal dryness, mood swings	reduced ovarian follicles
earlier cognitive function decline	infertility



PREMATURE OVARIAN FAILURE CAUSE

Possible factors involved in its development include genes, metabolism, endocrine, paracrine, and mitochondrial dysfunction-related factors, and autoimmune responses.
In addition, also chemotherapy, radiotherapy and surgery can contribute to POF; in particular, chemotherapy has been proposed to exert an indirect toxic effect on oocyte via cells surrounding it (stroma and granulosa cells).
The results are dysfunction and depletion of follicles, the sacs in the ovary that contain one immature egg each and that release a mature egg during ovulation.
The consequent loss of ovarian reserve increases the risk of infertility. Moreover, POF increases the risk of symptoms and health problems typically associated with menopause too.

OVOSKILL INCREASE THE SUCCESS RATE IN **IVF**

TREATMENT OPTION of choice is hormone replacement therapy. However, it does not restore ovarian function; that's why women looking for a pregnancy have to rely on infertility treatment. Moreover, hormone replacement therapy has been associated with the risk of breast and endometrial cancer. However, researcher have also being investigating possible ways to restore ovarian function. In this scenario, **Adipose Derived Stem Cells** - a multipotent cell type characterized by self-renewal capacity and able to differentiate into different cell types - represent a new tool with a potential with no precedents.

Reducing level of FSH	Improvement of ovarian weight
Elevating level of E2	High IVF success rate
Repair damaged ovarian function	Resuming of mestruation
Promoting formation of follicles	Totally safe and stable results

SCIENTIFIC EVIDENCE

ADSC transplantation in women with premature ovarian failure following chemotherapy was shown to induce ovarian function recovery, improving both hormone production and ovarian structure. It improves endometrial thickness too, and was associated with a richer blood signal in the endometrium.

In a study of idiopathic premature ovarian failure, autologous stem cell transplantation allowed ovulation in 60% of treated women[1].

In another study, menstruation restarted three months after stem cell therapy in 20% of treated women, who regained ovarian reserve and the secretory function of a previously atrophic endometrium. The treatment allowed a woman to get pregnant and to give birth to a full-term healthy baby[2].

Finally, preliminary results of the ROSE (Rejuvenation of Premature Ovarian Failure with Stem Cells) clinical trial demonstrated that in women who completed autologous stem cell therapy serum estrogen levels increased[3] months after stem cells injection.

The effect lasted for at least one year, menopausal symptoms were alleviated, and menstruations resumed six months after the injection[3.3].

BIBLIOGRAPHY

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2. Edessy M et al. Acta Medica International. 2016;3(1):19-23. doi: 10.5530/ami.2016.1.7
3. Endocrine Society. 2018 Press Release. March 18, 2018. https://bit.ly/2JrAqz4

ADIPOSE DERIVED STEM CELLS THERAPY

OvoSkill, the stem cell therapy for premature ovarian failure is based on the collection of only 20 cc of fat during a quick and painless outpatient procedure.

Bioscience Laboratories receive the collected fat and expand the isolated stem cells in only two weeks, obtaining several hundred million of pure autologous cells that can be used for ovarian failure treatment as well as for other procedures. The cells that are not immediately utilized are frozen and cryopreserved for future treatment; cells are preserved for a minimum of two years, ready to be thawed for additional use. OvoSkill it is delivered through intra-ovarian injection of autologous Adipose Derived Stem cells (ADSCs), a type of stem cells capable of self-renewal and of differentiating into multiple cell types. Stem cell therapy tolerability and safety have been plenty demonstrated and the use of autologous stem cells mitigate any immunogenic concerns. Their efficacy in the treatment of premature ovarian failure has been demonstrated too.

STEM CELLS ACTION

- differentiation into granulosa and stromal cells
- balance the reproductive ovarian physiology
- secretion of angiogenic GF, vascular endothelial GF, placental GF, trasforming GF β
- secretion of anti-inflammatory cytokine
- reduction of germ and stroma cells apoptosis
- enhancement of the maturation of the ovarian follicle
- anti-fibrotic and angiogenic effect

Step by Step

Sampling
20cc of fat are collected in the course of an outpatient procedure (quick and painless).

Extraction
The collected fat is received and processed at cGMP grade Bioscience Institute Laboratories.

Expansion
Several hundred milion of cells are produced in few week. Cells that can be used to perform different treatments.

Treatment
The vials can either be used to perform an immediate treatment, or they can be stored for future treatments.

Banking
The remaining vials are frozen and cryopreserved for minimum 2 years.

Thawing
The cryopreserved vials are ready to be used for additional treatments.

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