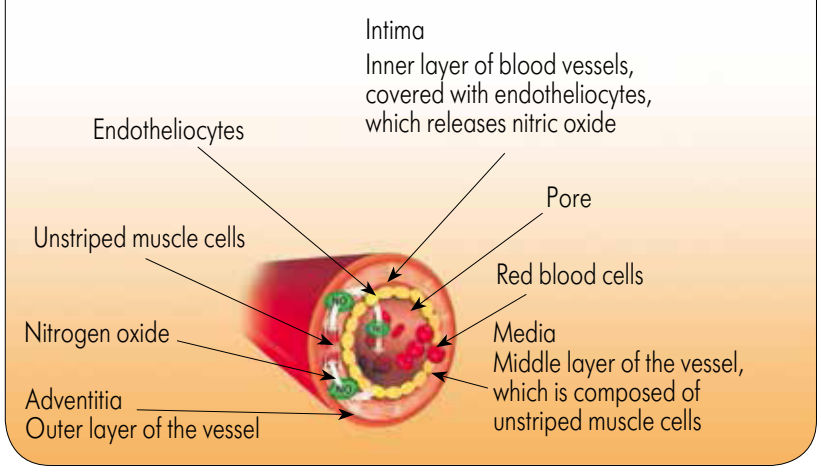
Reproductive results improving: L-arginine potential

L-Arginine: General Information

- Arginine (δ-guanidine-α-amino valeric acid, abbreviation – Apr, Arg, R) is basic α-amino acid, which L-form is a component of 20 amino acids that are encoded by the genetic code and form the basis of proteins.
- L-Arginine is half indispensable amino acid for a human: there are biochemical ways for its biosynthesis, but at certain life periods, particularly in the periods of intensive growth and development, as well as during some diseases, they cannot provide a sufficient amount of this compound, that is why it has to get into organism with food or as pharmaceutical products.
- Many experimental and clinical studies have demonstrated that exogenous oral L-arginine reduces the risk of cardiovascular disease, boosts the immune system, reduces the levels of "markers of aging" (asymmetric dimethyl arginin, homocysteine and malondialdehyde), protects the gastrointestinal tract, contributes to the recovery of damaged tissues, increases insulin sensitivity of tissues, improves cognitive function.
- It plays an important role in cell division, wound healing, immune function, hormone release, elimination of ammonia.
- It is a direct substrate for nitric oxide (NO) synthesis.
- It's a precursor of urea, ornithine, agmatine; required for the synthesis of creatine.
- It accelerates repair of damaged tissues.
- It normalizes high blood pressure.
- It is a powerful protein kinase mTOR agonist that regulates growth and metabolism at the level of cells and body.

L-arginine is the only source for the synthesis of nitric oxide (NO), necessary for normal functioning of all vessels



Integrative role of L-arginine in Human Reproduction

L-arginine

Fertilization
- Corrects luteal phase deficiency
- Promotes embryo implantation
- Improves blood supply to the endometrium

Sexual Health and Fertility
- Delays aging
- Increases testosterone level in men
- Reduces the risk of endometriosis, polycystic ovarian syndrome, inflammatory diseases of the pelvic organs in women
- Modulates oocyte maturation and steroidogenesis
- Modulates ovulation

Normal pregnancy
- Improves survival rates of embryo and fetus
- Improves the growth of the uterus and placenta
- Improves the function of the placenta
- Improves fetal growth
- Reduces the risk of preeclampsia
- Improves the results of Apgar assessment

Complicated pregnancy
- Increases the frequency of live birth, as well as baby's weight at birth and prolongs pregnancy in case of intrauterine growth retardation
- Improves the results of Apgar assessment in case of preeclampsia
- Reduces blood pressure in women with gestational hypertension

Childbirth
- Corrects placentofetal blood flow in case of premature birth, reduces the frequency and intensity of uterus involution

Neonatal period
- Reduces the incidence of necrotizing enterocolitis, infections and chronic lung disease in premature newborn

Fertility and the role of L-arginine

! L-arginine can increase the level of testosterone in men with erectile dysfunction, it acts synergistically with testosterone in men with hypogonadism.

! L-arginine is a promising drug in the combination treatment and prevention of relapse of endometriosis, polycystic ovarian syndrome, inflammatory diseases of the pelvic organs.

! In women with polycystic ovarian syndrome a combination therapy with L-arginine 1600 mg/day contributed to restoring gonadal function likely by improving insulin sensitivity (A. Masha et al., 2009).

Assisted reproductive technology

- Optimizes traditional progesterone treatment of luteal phase deficiency.
- Acts synergistically with gestogens.
- In irresponsive women it improves the response of ovarian, endometrial receptivity and frequency of pregnancies.

Adjuvant therapy with L-arginine in *in vitro* fertilization

In medical history of women with low ovarian response oral L-arginine may improve the response of the ovaries, uterine blood flow, endometrial receptivity and frequency of pregnancies.

In this study Battaglia et al. explored the role of L-arginine in improving uterine blood flow and ovarian response to gonadotropin in irresponsive women with unsuccessful ***in vitro*** fertilization in medical history. Patients were divided into two groups, depending on stimulation protocol: gonadotropin releasing hormone analogue (GnRH) triptorelin 0.1 mg subcutaneously starting on Day 1 of menstrual period + purified follicle-stimulating hormone (FSH; 450 IU intramuscularly in the first 3 days of menstrual period, then individual doses) or triptorelin + FSH + L-arginine 16 g orally. If there was at least one follicle > 17 mm in diameter, triptorelin, FSH and L-arginine were discontinued and 10,000 IU of human chorionic gonadotropin (HCG) was administered.

NB! ***As it was defined by ESHRE (European Society of Human Reproduction and Embryology), irresponsive women are women having at least two of the following three factors: 1) the older age of the mother or any other risk factor for poor ovarian response; 2) previous poor ovarian response and 3) abnormal test results for follicular ovarian reserve.***

Following results were obtained in the process of the study:

✓ no significant side effects in the group of L-arginine;

✓ significantly lower frequency of stimulation protocol termination in the L-arginine group as compared with control group (11 vs 76%, p <0.001);

✓ no pregnancies in the control group and 17% of pregnancies in the group of L-arginine;

✓ group of L-arginine experienced significantly higher plasma concentrations of estradiol and growth hormone on the day of HCG administration;

✓ L-arginine concentration in plasma positively correlated with the number of follicles developed and negatively correlated with PL of uterine and perifollicular arteries (the lower PL is, the better uterine blood flow and tissue perfusion are);

✓ group of L-arginine showed thicker endometrium (0.95 vs 0.75 mm), more collected follicles (4.1 vs 1.6) and more transferred embryos (2.4 vs 1.0).