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**Infertility - causes, diagnosis, preventive measures and methods of treatment**

Aleksandra Mazurek Uniwersytet Medyczny im. Karola Marcinkowskiego w Poznaniu aleksandramazurek7@gmail.com

Damian Machaj Uniwersytet Medyczny im. Piastów Śląskich we Wrocławiu damian10b10@o2.pl

Jakub Polak Śląski Uniwersytet Medyczny, Wydział Nauk Medycznych w Zabrzu kubap99@op.pl

Daniel Grobecki Uniwersytet Medyczny im. Piastów Śląskich we Wrocławiu danielgrobecki00@gmail.com

Jakub Lis Uniwersytet Opolski jlis2607@gmail.com

Dominik Machaj Uniwersytet Medyczny w Lublinie dominik5a4@tlen.pl

Przemysław Raczkiewicz Uniwersytet Medyczny w Lublinie 600700200x@gmail.com https://orcid.org/0000-0002-4986-4833

Weronika Adamik Uniwersytet Opolski weronika.adamik@onet.pl

**Summary**

The problem of infertility affects approximately 20% of married couples, and the number of people affected by this problem is still increasing[5,6]. Developed countries are characterized by the prevalence of primary infertility, while in developing countries there is a high rate of secondary infertility[8,9]. The most common cause of marital infertility is obstruction of the fallopian tubes, which occurs in 30-35% of women and requires surgical intervention. However, both sexes are dominated by immunological and hormonal disorders (25%-30% of cases)[3,4]. The basic examination in which male fertility is determined is the semen analysis, while in women, many tests should be performed in order to make a diagnosis: anamnesis, gynecological examination, ultrasound performed repeatedly during the menstrual cycle (ovulation assessment), hormonal and immunological tests, post-coital tests, bacteriological cultures, hysterosalpingography or laparoscopy [20]. In vitro fertilization is the most effective of all methods of infertility treatment. In vitro fertilization can be performed using the classical method by adding prepared sperm to the egg cells or by microinjection of the sperm into the egg cell[21].

**Key words:** infertility, spermiogram, in vitro fertilization,

**Introduction and Purpose**

Nowadays, infertility is defined by the World Health Organization (WHO) as the inability to get pregnant despite regular sexual intercourse (i.e. 3-4 times a week), maintained for more than 12 months, without any preventive measures [1,2]. There is primary infertility (in the case of inability to conceive), which affects women who have never been pregnant, and secondary (if pregnancy occurs and ends in miscarriage and women are unable to become pregnant again). Secondary infertility also includes cases when women have no problem getting pregnant, but due to the inability to carry it to term, they end up with miscarriage or premature birth [3,4,5]. It is estimated that the problem of infertility affects about 60-80 million women worldwide, and there are another 2 million every year. According to various sources, infertility affects 20% of married couples in the world and occurs, for example, in the USA in 13-14% of couples, in France in 18.4%, in Great Britain in 16.8%, while the highest percentage is found in African countries and South America [5,6]. In Poland, it is estimated that infertility affects almost 2.4 million women and men (with a population of almost 38 million in this country), with 40% affecting women, 40% men, and the remaining 20% are causes that depend on from both partners or are unexplained (5,7). The aim of the work is to present the main causes of infertility among women and men, to discuss the principles of diagnosis and prevention as well as methods of infertility treatment.

**Description of the state of knowledge**

Developed countries are characterized by the prevalence of primary infertility, while in developing countries there is a high rate of secondary infertility. The main reasons for the high rate of secondary infertility in developing countries are sexually transmitted diseases and surgical interventions in women in the postpartum period, undertaken in conditions devoid of any sanitary and epidemiological standards [8,9]. The causes of infertility are very complex. Chronic stress, improper nutrition or excessive physical and mental effort cause hormonal disorders in both women and men, and these can lead to anovulatory cycles and deterioration of biological semen quality parameters. The most common cause of marital infertility is obstruction of the fallopian tubes, which occurs in 30-35% of women and requires surgical intervention. On the other hand, both sexes are dominated by immunological and hormonal disorders (accounting for 25%-30% of cases), which, in addition to thorough diagnosis and treatment by specialists in various fields of medicine, also require appropriate eating habits and often lifestyle changes[8]. In the case of the 'male factor' of partner infertility, it is assumed to be responsible for 40-60% of all detected cases of infertility [3,4]. The inability of men to fertilize may be the result of the existence of mechanical obstacles in getting out of the right amount of properly formed sperm and disorders of spermatogenesis and spermiogenesis. The reason for mechanical obstacles may be developmental disorders, physical injuries, as well as the remains of inflammation (e.g. after a history of venereal diseases). Disturbances in the process of spermatogenesis may result from both developmental and hereditary changes (usually abnormal location of the testes outside the scrotum), but they can also be caused by primary or secondary damage to the testicles. The causes of male infertility (which can be divided into testicular, pre-testicular and extra-testicular) are: erectile dysfunction, lack of vas deferens or their obstruction, impaired sperm transport, developmental or congenital testicular disorders, systemic disorders, testicular injuries, varicocele, obstruction or absence of the epididymis, and the effects of certain medications. Factors that increase the risk of infertility in men include: smoking and alcohol abuse, exposure to high levels of radiation, exposure to heavy metals, drug use, use of anabolic steroids, organic chemicals and high ambient temperature. The ability to fertilize in women depends on the correct regulation of the hypothalamic-pituitary-ovarian axis, the occurrence of ovulation and the production of the corpus luteum, which produces hormones that support the development of early pregnancy. The next stage involves the capture of the egg by the hyphae of the fallopian tube and transport through the patent fallopian tube, where fertilization takes place. Then the zygote is implanted in a properly built uterus, whose mucous membrane is transformed, among others, into due to the proper functioning of the corpus luteum. Disturbance of any stage causes fertility disorders in women and difficulties in conceiving a child [8]. Female infertility can be caused [8] by: endometriosis, obstruction of the fallopian tubes, ovulation disorder, uterine or cervical factor, diseases of infectious and immunological origin. Factors that increase the risk of infertility in women include: [10; 11]: smoking and alcohol abuse, stress, surgeries, organic chemicals, excessive noise, the influence of certain medications (e.g. hormonal), as well as bad eating habits. The causes of infertility in both men and women include all infections within the pelvic organs, i.e. orchitis or appendicitis of various etiology [8]: mumps or gonococcal orchitis, syphilis, Chlamydia trachomatis, Mycoplasma sp. These factors include systemic diseases such as [12]: diabetes, anemia, chronic nephritis, cardiovascular or thyroid diseases, but also eating disorders. These problems with proper nutrition are often associated with excessive consumption of carbohydrates. The result of the situation when their concentrations are too high is the imbalance of hormones responsible for fertility, and this causes ovulation disorders. Insulin secreted by the pancreas together with the accompanying insulin-like growth factor (IGF-1) inhibits the production of the protein responsible for binding sex hormones (especially male) in the blood. When the protein concentration is too low, male hormones (mainly testosterone) begin to predominate in a woman's bloodstream, leading to a disruption of the subtle hormonal balance. This situation occurs when the diet is dominated by industrially processed and easily digestible carbohydrates, which include white ones bread, pasta, noodles, rice, sweets and sweet carbonated drinks. The products listed above should be replaced by: unprocessed, fiber-rich wholemeal bread, wholemeal pasta, paddy rice, legumes and fresh vegetables and fruits[5, 13]. Consumed protein has a similar effect on blood sugar and insulin levels, and thus on the concentration of insulin-like growth factor. Research conducted at the Harvard School of Public Health on the link between the consumption of plant and animal protein and infertility caused by ovulation disorders shows that women who consumed more animal protein than vegetable protein were at a higher risk of infertility[5, 14]. The woman's hormonal balance is also disturbed by the consumption of skimmed milk products. This is because these products contain lower amounts of vitamin D, which is a steroid compound that affects fertility. However, it should also be noted that the technological processes that take place during the removal of fat from milk change its hormonal composition, which reduces the estrogen and progesterone content, while leaving an excess of male hormones that interfere with ovulation (5,15). There are few scientifically reliable reports on the effect of supplementation on infertility caused by ovulation disorders. Research conducted by Chavarro et al., which is one of the few, suggests that women who took iron supplements at a dose of at least 40 mg / day had 40% less problems with getting pregnant. It should be noted, however, that this fact concerned only women consuming iron from vegetables, fruits and supplements (5,17). Other studies suggest that the frequency of ovulation and conception may increase with a folic acid intake of 700 μg/day (compared to the generally recommended standard of 400 μg/day) (18). In addition to a proper diet, prophylactic activities related to infertility include (especially in relation to women): maintaining a normal body weight and physical activity. Obesity at a young age may lead to menstrual disorders, anovulatory cycles and infertility in adulthood, while obesity at childbearing age may be associated with a reduction in reproductive potential in previously ovulatory women [5]. In addition, studies by Rich-Edwards et al. confirm the fact that an hour of exercise a day can positively affect fertility in women[16]. For men, doctors recommend wearing loose-fitting underwear and refraining from using heated car seats to protect the gonads from high temperatures[19].
The basic test in which male fertility is determined is the semen analysis. Prior to semen collection, the man is required to abstain from sexual and alcohol consumption, which lasts from two to seven days. Semen is obtained by masturbation (in a special room near the laboratory) into sterile and screw-cap containers made of plastic, which has no toxic effect on semen. According to the recommendations, men should wash their hands and penis thoroughly before donating semen. Semen containers are heated to 37°C. The signed and sealed containers of semen samples are then delivered to the laboratory at a temperature between 20 and 40°C. A person taking care of a man diagnosed with potential infertility should be able to properly interpret the semen analysis result according to the criteria developed by the WHO. It must also take into account the fact that a single spermiogram does not conclusively prove a man's fertility. The occurrence of diametrically different semen parameters in the same man at different time intervals is not a pathological phenomenon. At the same time, the only certain confirmation of a man's fertility is the fact that his partner is pregnant. In the case of abnormal semen analysis results, diagnostics should be extended to include such tests as hormonal determinations, bacteriological, ultrasound, genetic and immunological tests. The person ordering the test should also take into account the age of the couple being treated, because too long a diagnosis may result in the spouses losing their reproductive abilities (the effectiveness of treatment decreases with age). Performing a spermiogram according to WHO standards is a screening test. Patients with abnormalities should have a hormonal profile including prolactin, FSH, LH, and testosterone. Routine semen analysis includes volume, viability, concentration, percentage of motile sperm in each class, morphology, and leukocyte count. One of the causes of male infertility are hormonal disorders manifested in the spermiogram by reduced semen density. They can be associated with FSH and LH deficiencies, which is due to the reduction the production of these hormones by the pituitary gland. Infertility resulting from pituitary disorders is treated with supplementation of pituitary gonadotropins or HCG, which similarly stimulates spermatogenesis. A decrease in sperm density may also be the result of hyperprolactinaemia, which is treated with bromocriptine. Finding signs of inflammation in the spermiogram (by observing an increase in the density of leukocytes or an increase in pathogenic bacteria in the semen culture) is an indication for antibiotic therapy and eradication of the infection. In the case of a bacterial infection in a man, a bacteriological culture should be performed on his partner and treatment should be started at the same time.
On the other hand, in women, in order to make a diagnosis, many tests should be performed: interview, gynecological examination, ultrasound performed repeatedly during the menstrual cycle (ovulation assessment), hormonal and immunological tests, post-coital tests, bacteriological cultures, hysterosalpingography or laparoscopy. At the moment, there is no diagnostic minimum that would define the smallest scope of necessary tests. The choice of diagnostics depends on the results of tests obtained on an ongoing basis in the woman and her partner, as well as on the treatment options that the couple may choose[20]. The most effective method of infertility treatment is in vitro fertilization, which is the method of choice in couples with: irreversibly damaged fallopian tubes or their absence, moderate and advanced grade III and IV endometriosis, and severe male factor (with severe oligoasthenozoospermia or azoospermia with preserved spermatogenesis) . This method is also indicated in the next stage of management, when conservative or surgical treatment is ineffective in couples with: moderate male factor, grade I and II endometriosis, unexplained infertility, tubal factor, or ovulation disorders. IVF is also recommended for fertile couples in certain cases. These cases include: delayed fertility due to medical indications, as well as carriers of recessive genetic changes by both partners (which cause severe, irreversible defects or diseases in the offspring). In vitro fertilization can be performed using the classical method by adding prepared sperm to the egg cells or by microinjection of the sperm into the egg cell[21]. The effectiveness of infertility treatment by in vitro fertilization largely depends on the result of controlled ovarian hyperstimulation - COH. Its purpose is to enable the collection of the optimal number of mature oocytes[21,22].

**Conclusions**

1. The causes of male infertility can be divided into nuclear, pretesticular and extratesticular, and the ability to fertilize in women depends on the correct regulation of the hypothalamic-pituitary-ovarian axis.
2. Preventive actions include, among others: appropriate diet and supplementation, physical activity, avoiding chronic stress, alcohol and smoking.
3. The basic examination in which male fertility is determined is semen analysis, while the selection of diagnostics in women depends on the results of tests obtained on an ongoing basis in the woman and her partner, as well as on the treatment options that the couple may choose.
4. Among all methods of infertility treatment, the method of in vitro fertilization is the most effective.

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