



## **STERILIS - THE MOST IMPORTANT MEDICAL, SOCIAL AND DEMOGRAPHIC PROBLEMS**

**Saparbayeva Nasiba Rakhimbayevna**

Assistant, Department of Obstetrics and gynecology,  
Urgench branch of Tashkent Medical Academy, Urgench, Uzbekistan

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<b>Received:</b> January 10 <sup>th</sup> 2022 <b>Accepted:</b> February 10 <sup>th</sup> 2022 <b>Published:</b> March 24 <sup>th</sup> 2022	Preservation and restoration of reproductive health is the most important medical task of national importance. Therefore, modern diagnostics with subsequent treatment of infertility should be regarded as a reserve for the birth of desired children and an increase in the reproductive potential of the population. In order to systematize the most rational and reliable methods for examining infertile couples to clarify the causes of infertility and determine treatment tactics, a review of modern specialized literature was carried out. It was established that the mandatory methods for diagnosing infertility are a thorough history taking, examination, clinical, ultrasound, instrumental, radiological, pathohistological, genetic. It should be noted that infertility is a condition that characterizes a couple, and not a separate organism, so diagnostic algorithms should consider both partners.

**Keywords:** Infertility, Reproductive Dysfunction, Examinations, Folliculometry, Spermogram.

Sterilis - is one of the most important medical, social and demographic problems of our time. A marriage is considered infertile if pregnancy does not occur within a year of regular sexual activity without the use of contraception [5]. The world's frequency infertility ranges from 8% to 29% [5].

In the Khorezm region over the past 10 years, there has been an increase in reproductive disorders in women and men. Over the past 3 years, the number of women of reproductive age has decreased by 13,725 people in the region. The number of infertile couples is 20% (in Uzbekistan - 15%).

Pregnancy and childbirth, feeding, raising a child are incomparable factors in terms of the strength of a positive effect on the body. Infertility is the cause of painful experiences for spouses and a difficult test for the marital union [1].

### **OBJECTIVE**

Based on the data of modern specialized literature, to systematize and present an algorithm for the most rational and reliable methods for examining infertile couples to clarify the causes of infertility and determine the tactics of further treatment. The high rate of infertility is a reflection of the catastrophic decline in reproductive health population [12]. According to the WHO, reproductive health is "a state of complete physical, mental and social well-being, providing the opportunity to lead a safe and effective sexual life, in combination with the reproduction of offspring at a time and in the amount determined by the individual".

Unfortunately, our contemporaries are subject to a number of negative factors, sometimes irreversibly reducing their reproductive potential. We are talking about both environmental factors and lifestyle features. Depending on the damaging factor, certain parts of the reproductive system fail [5].

Often the cause of infertility is not one, but several factors. Therefore, the task of a doctor examining an infertile couple is to establish all the causes of infertility and determine the shortest and most rational way to overcome the problem, taking into account the optimal expenditure of time and material resources of the family [5]. It should be noted that infertility is a condition that characterizes a couple, and not a separate organism. Therefore, diagnostic algorithms must consider both partners. It has been established that the frequency of male and female infertility is almost the same. Approximately one third of cases of infertility in a couple are caused by causes on the part of the woman, the same number on the part of the man, in the remaining cases, the pathology is found in both partners [15].

Examination of a married couple by infertility specialists (fertility doctors) includes a joint examination of the husband and wife to assess the state of the reproductive function of the spouses. Working with both spouses allows you to outline a general survey plan.

A married couple should be warned that the average pregnancy rate is 30-35%, and that after a complete clinical and laboratory examination in 5-10% of couples, the cause of infertility remains



unexplained. In most cases, it is possible to establish the cause of infertility with a comprehensive examination of infertile couples. At the same time, it is important to properly organize and establish a phased diagnosis and treatment of spouses. Examination of infertile couples should be carried out according to the plan within several months (2-3 months, maximum 6 months) [18].

**At the WHO symposium** (1976), a scheme for a comprehensive examination of a married couple was proposed, consisting of **5 stages**.

- **Stage I** includes the collection of anamnesis and examination of the couple. All factors related to the occurrence of infertility are clarified (somatic history, previous surgeries, infections, the nature and characteristics of the development of sexual function, social conditions, possible adverse effects of external factors on the state of the reproductive organs, etc.). At this stage, women undergo a gynecological examination, ultrasound of the pelvic organs. At the same time, a comprehensive examination of the husband and infectious screening of both spouses are carried out;

- **Stage II** - confirmation of ovulation by various methods (studying the nature of basal temperature graphs, determining the level of sex hormones, taking an endometrial biopsy, other functional diagnostic tests to assess ovarian activity, ultrasound folliculometry);

- **Stage III** - the study of cervical mucus and sperm, as well as their compatibility. Tests are carried out to study the nature of the mucus of the cervical canal and determine the degree of penetration of spermatozoa into the mucus of the cervical canal in vitro and in vivo (TKSTSS, PCT);

- **Stage IV** includes determining the patency of the fallopian tubes. The study is carried out on an outpatient basis or in a hospital (laparoscopy, hysteroscopy, hysterosalpingography, etc.);

- **Stage V** - conducting special research methods to confirm the pathological changes established at the previous stages.

#### **ANAMNESIS AND EXAMINATION OF A MARRIED COUPLE**

The completeness of the collection of patient complaints allows us to suspect one or another hormonal dysfunction [1,5,12].

The initial survey of each couple is a very important stage of the survey, as it allows you to get an idea of the possible causes of infertility on the part of men and women, taking into account their interaction. A detailed medical history of the couple includes past illnesses (therapeutic, surgical, gynecological, infectious, endocrine, etc.), social conditions, possible

harmful effects, the formation of menstrual, sexual function.

It is necessary to clarify the features of the psychological, emotional and sexual behavior of both partners. Important aspects of women's medical history: duration of infertility, menstrual function, presence and characteristics of previous pregnancies, presence of pregnancies with other partners, previous contraception, frequency of sexual intercourse and presence of sexual dysfunctions, gynecological, somatic diseases and operations, medications, results and methods of previous infertility treatment.

Important aspects of the **anamnesis** in men: the duration of infertility, whether there were pregnancies in relationships with other women, past diseases and surgeries, medication, alcohol abuse, drug abuse, smoking, exposure to physical factors (thermal, chemical, radiation), sexual dysfunction, wearing thick underwear, frequent hotbaths, saunas, results and methods of previous fertility treatments.

**The objective status** of patients is very important: it is necessary to determine the height, body weight, appearance, physical characteristics and conduct a general medical examination [9,14].

**Ultrasound research.** Ultrasound of the pelvic organs is performed for all patients with infertility on the 5-7th day of the menstrual cycle. The study allows diagnosing neoplasms and anomalies in the development of internal genital organs, as well as intrauterine pathologies. Breast ultrasound is a non-invasive screening method for examining women with infertility under the age of 35 choleform formations before the forthcoming hormonal therapy.

**Mammography** is an x-ray method of examination, which is carried out according to the indications, depending on the data of the clinical examination and ultrasound. In patients older than 40 years, mammography is a more informative method of examination compared to ultrasound of the mammary glands.

Due to the high incidence of inflammatory diseases of the genital tract in women of childbearing age and their negative impact on the state of the reproductive system, it is necessary to examine all women with infertility for the presence of sexually transmitted infections (STIs) [20,21].

Folliculogenesis is an **ultrasound** study carried out during the menstrual cycle. It allows, already on the 7th–9th day of the menstrual cycle, to note the appearance of a maturing follicle in the ovary in the form of an echo-negative rounded formation with an average diameter of 8–10 mm, which by the middle of the menstrual cycle increases to 19–22 mm (maximum 25 mm, on average 2–3 mm/day). One of



the signs of the onset of ovulation is the appearance of free fluid in the retrouterine space, the absence of a dominant follicle and the appearance of a corpus luteum in its place.

**To check the patency of the fallopian tubes, a series of tests is used, which in some cases complement each other:**

- **Hysterosalpingography (HSG)** - X-ray method of research using X-ray contrast substances;
- **Fertileoscopy** - examination of the pelvic organs by inserting an endoscope through the posterior Douglas;
- **Laparoscopy** is an invasive research method that allows you to visually examine the uterus and tubes with sides of the abdominal cavity. Chromosalpingoscopy is performed to determine the patency of the fallopian tubes [6,12,13,24];
- **Echohydrotubation** – an ultrasonic research method with the use of echocontrast agents;
- **Pertubation** - blowing the fallopian tubes with carbon dioxide or air under pressure control.

**Laboratory research.** Due to the fact that cervical factors as a cause of infertility are quite common (3–15%), their study should begin with determining the amount of mucus, pH, viscosity, extensibility, and the presence of cells.

A vaginal smear is examined to determine the degree of purity, vaginal contents - to assess microbiocenosis, a smear from the cervical canal - to detect chlamydia, ureaplasmas, mycoplasmas, herpes simplex virus (HSV), cytomegalovirus (CMV) by polymerase chain reaction (PCR), blood - for research on toxoplasmosis (with a history of habitual miscarriage).

To assess the hormonal activity of the ovaries and confirm ovulation is currently used home test for ovulation Cliaplan, based on the reaction to the preovulatory release of luteinizing hormone into the urine. It is also informative to study the graph of basal temperature.

It is necessary to determine the phenomenon of cervical mucus crystallization, a symptom of the "pupil" [1,5,7].

**The postcoital test (PCT)** is an available screening test to assess the biological compatibility of spermatozoa and cervical mucus. It is necessary to conduct PCT according to the standards, since ignoring them leads to false results, and hence to unsuccessful treatment.

**Sperm-cervical mucus contact test (SCMCT)**

If the index of the postcoital test is less than 30, then with the help of SCMCT, the penetration ability of spermatozoa is studied.

In modern reproductive immunology, 5 categories of immune problems have been identified that are the causes of reproductive losses and often exist in combination [26]: HLA-compatibility of partners, thrombophilia, anticlear antibodies to DNA and histones of fetal and placental tissues, antisperm antibodies in sexual partners, improved quality and activity of some immune cells, natural killers (NK) in the blood, determination of DM 57 cells in the uterus, the appearance of antibodies to hormones and antibodies to neurotransmitters.

Indications for conducting immunological studies of a married couple: autoimmune diseases thyroid gland, insulin resistance, diseases of the cardiovascular system, chlamydia, depression, chronic fatigue syndrome, infertility of unknown origin. The reproductive immunological phenotype, the Th1/Th2 ratio, the presence of antisperm antibodies in the blood are determined, the MAR test, PCT, and SCMCT are performed.

Immunological disorders in the process of sperm fertilization and early embryogenesis are associated with the presence of specific antibodies to gametes, in particular to spermatozoa.

Spermobilizing, spermoluteinating, spermolizing antisperm bodies (SLAB) are distinguished. They can be found in the blood serum, various secrets of the reproductive system (cervical mucus, ejaculate) in one or both sexual partners. Currently, the main screening immunological method of examination is the MAR test, with which determine SLAB in the ejaculate. The presence of SLAB indicates the presence of the immune factor of infertility. The norm for the MAR test is less than or 30%. The MAR test values exceeding 30% serve as the basis for establishing the diagnosis of the immunological form of infertility in the husband and for treatment with the help of artificial insemination with the husband's sperm (IUI) or in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI).

**Special research methods** include [2,7,8,11,17]:

**Hormonal screening.** Endocrine disorders can be both an independent cause of infertility, and a factor accompanying any other cause. If women have an unchanged menstrual cycle at the initial stage, it is sufficient to determine progesterone, prolactin and testosterone. With oligo- and amenorrhea, it is mandatory to determine in the blood plasma prolactin, follicle-stimulating, luteinizing, thyroid-stimulating hormone, estradiol (E2), testosterone, cortisol, DEA-S, triiodothyronine (T3), thyroxine (T4), according to indications - dehydroepiandrosterone (DEA) and 17-hydroxyprogesterone (17-OP).



**An X-ray of the skull and sella turcica** is performed in patients with menstrual irregularities for the diagnosis of neuroendocrine diseases. It is not very informative and has no independent value.

**Computed tomography and magnetic resonance imaging** are indicated for patients with an increase in plasma prolactin levels in case of suspected pituitary microadenoma.

**Ultrasound** of the thyroid gland is indicated for patients with menstrual irregularities of the type of oligo- and amenorrhea.

**In the diagnosis of male infertility, the main points can be distinguished [22].**

**Clinical methods:** primary survey (anamnesis), general medical examination, urogenital examination, examination by a therapist, geneticist, sexologist. Laboratory diagnosis of male infertility involves the study of ejaculate and prostate secretion. Reserve tests allow to determine the functional state of spermatozoons, regardless of spermogram parameters (resistance, redox ability, speed of movement, fatigue, duration of spermatozoon motility, number of sperm cells with rectilinear movement).

To assess the ejaculate, a macro- and microscopic examination is carried out, the concentration of spermatozoons, the number of mobile, living and pathological forms are determined, fructose and citric acid are also examined, the presence of inclusions (lecithin grains, epithelial cells, leukocytes, erythrocytes, spermatozoons, etc.) ). Given the undulating nature of spermatogenesis, the ejaculate should be examined 2-3 times with an interval of 1-2 weeks and at the same time focus on the best indicators. The results of the study are recorded in the ejaculate analysis form.

To assess the fertilizing ability of the ejaculate, WHO proposed to use the concept of "fertile pool", which means the minimum number of live, orphologically normal and well-motile sperm, sufficient to fertilize the egg. The size of the fertile pool is 20 million sperm with normal characteristics. The presence of a fertile pool in the patient's ejaculate indicates a preserved fertilizing ability.

The secret of the prostate gland is obtained by the method of finger massage of the prostate after 2-3 days of abstinence from sexual activity, a native drop is examined. The presence and amount of lecithin grains, leukocytes, epithelium, erythrocytes, spermatozoons, microflora, Trichomonas, etc. in the secret are determined.

Laboratory and diagnostic methods for determining the causes of male infertility: testing for chlamydia, ureaplasmosis, mycoplasmosis, HPV, bacteriological analysis of semen, determination of

ASAT, ultrasound of the pelvic organs, ultrasound of the thyroid gland, thermography of the scrotum, hormonal screening, medical genetic testing, X-ray methods (research of the skull, renal phlebography), testicular phlebography.

**Additional examinations to clarify the diagnosis of male infertility:**

**1. Excretory infertility:** urinalysis in 3 portions; bacteriological studies of urethral secretions, urine, semen, prostate secretion for the presence of pathogenic and saprophytic microorganisms, fungi, mycoplasmas, ureaplasmas, scraping of the urethra for the presence of

chlamydia, trichomoniasis; RSK blood with chlamydial antigen, with monoclonal antigens; functional tests with spermatozoa, paired tests. If obstruction is suspected, a 3-fold study of the ejaculate is carried out for the presence of spermatogenesis cells in the centrifuge. In the absence of spermatogenesis cells, genitography with simultaneous testicular biopsy is indicated. Gonadotropic hormones are also examined.

**2. Secretory infertility:** biochemical study of ejaculate, fructose, citric acid, fructolysis, trace elements. Determination of the excretion of sex hormones (FSH, LH, T, PRL, 17-KS, estrogens) and their fractions; functional hormonal tests with hCG, with hCG and dexamethasone. Carry out cytogenetic studies (sex chromatin, karyotyping), study of the function of the adrenal glands, liver, thyroid gland, sympathetic-adrenal system (catecholamines), basal metabolism, x-ray and vascular studies, testicular biopsy (if indicated). Medical genetic consultation is required.

**3. Combined infertility** occurs when a combination of 2 or more factors of infertility, depending on which. Appropriate additional diagnostic methods are applied.

**4. Immunological infertility:** determination in the ejaculate of the degree of spermagglutination and the number of spermatozoa with rocking and pendulum movement, PCT, TKSS (direct and cross), ASAT in semen, cervical mucus, blood serum of spouses, SIAT (sperm immobilizing antibodies according to Kibrick), CAAT (sperm agglutinating antibodies according to Izojima and Lehmann). Use indirect immunofluorescent method, immunogram, etc.

**5. Relative infertility:** sexological, urological, gynecological, instrumental and X-ray examinations, examination of postcoital urine, etc.

**6. Psychogenic infertility:** psychological, pathopsychological, psychiatric examination, elucidation of possible hidden mechanisms of psychogenicity [23].

Cytogenetic studies should always be resorted to if patients with primary amenorrhea and patients with



grade III–IV oligozoospermia come to the clinic. (less than 5 million spermatozoa in 1 ml of ejaculate), azoospermia and aspermia.

Approximately 4% of patients with primary amenorrhea establish deviations of the genetic plan. Most often in women, these are various variants of Turner's syndrome, testicular feminization syndrome, but there may also be variants of "pure" gonadal dysgenesis. Violation of the genetic code in men is most often Klinefelter's syndrome (1:400–1:500 in the population).

### CONCLUSIONS

1. Sterilis (infertility) - is a pathological condition that in most cases can be treated. A properly developed diagnostic algorithm allows you to solve the issues of implementing the reproductive function in the optimal time frame.
2. Infertility is a condition that characterizes a married couple, and not a separate organism. Diagnostic algorithms should consider both partners.
3. A carefully collected anamnesis, examination, clinical, ultrasound, instrumental, radiological, pathohistological, genetic research methods should be performed to clarify the diagnosis.
4. Given that the examination of fertile couples is a physical and emotional burden, all consultations should aim to form a positive working relationship to determine the purpose and algorithm of the examination of the married couple.

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