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Cryptorchism is the Main Cause of Male Infertility (Review)

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Abstract: *The frequency of occurrence of cryptorchidism in children is presented. The leading methods of diagnosis and treatment of congenital pathology are considered, first of all ultrasound examination, the reliability of which reaches 88% when the testicle is palpated.*

Relevance*. Currently, there are about 250 methods of surgical treatment of an organ position anomaly. The most widely used ones are Petriwalsky-Shoemaker and Fowler-Stephens, which are performed in one or two stages. In some cases, hormone therapy is resorted to using chorionic gonadotropin, less often gonadotropin-¬releasing hormone, but the effectiveness of this therapy does not exceed 15% and depends on the height of the testicle in the inguinal canal. With agenesis (aplasia), testicle prosthetics are performed with silicone implants in order to eliminate the psychological and cosmetic defect. When analyzing the results of correction of pathology in patients, there is a violation of fertility up to 50%, even with timely reduction of testicles. Preventive examinations of adolescents, dispensary monitoring of a group of operated patients with the appointment of ultrasound examinations and the study of hormonal status will help to increase the reproductive potential of the male population.*

Keywords: *cryptorchidism; testicular misalignment; testicular prolapse; hypoplasia; fertility.*

Diseases associated with the pathology of the inguinal canal, more often than other surgical problems in children's practice, require planned surgical treatment andleave more than 33% [1,4]. At the present stage, specialists are improving surgical treatment technologies, setting themselves the task of reducing surgical injuries and reducingthe number of complications [5]. Cryptorchidism is a systemic disease, one of the external manifestations of which is a violation of the migration process (malescentia) of the testicle from its original location (mesonephros) to the scrotum cavity.

In the ICD-10 classifier, cryptorchidism is in the class of diseases of the genitourinary system, category Q53. This pathology can be diagnosed at any age, occurs in 10-20% of newborns (up to 30% - in premature newborns), in 3% of one-year-olds, in 1% of cases atpuberty, in 0.3% of adult men [1]. Violation of the testicular position is also associated with pathology of the vaginal process of the peritoneum [1,2,]. It is known that the mesenchymal base, as a source of interstitial tissue, plays an important role in the process of hormonal regulation and testicular migration in the intrauterine period. The mesenchyme consists of fibroblasts that later differentiate into Leydigcells. It is the active production of dehydroepiandrosterone and testosterone by these cells that determines testicular migration from the abdominal cavity to the scrotum [3,4]. The scrotum is a thermoregulatory protector for normally located testis. It is remote from the body, has thin skin with no subcutaneous fat and an abundance of sweat glands. Due to its elasticity and the presence of a cremasteric reflex, the testicles are protected from the damaging effects of high temperatures. Therefore, for normal life, the testicles must be located in the scrotum. It is here that the most favorable temperature and life conditions are provided for the formation and maturation of spermatozoa, as well as for normal hormonal function [1, 5,].

Manifestations and consequences of cryptorchidism. OOne of the most important and severe consequences of cryptorchidism is a violation of the germinal function. Histological examination in undescended testicles reveals a decrease in the diameter of the seminal ducts, a decrease in the number of spermatogonia. Similar changes are detected in 90% of children over 3 years of age. Impaired fertility even with timely testicular reduction is noted in 50% of patients with bilateral and in 20% of patients. with one-way cryptorchidism. In the F. Hadziselimovic study [6], azoospermia was observed in 89% of untreated children with bilateral cryptorchidism. At birth, undescended testis have normal spermatogenesis cells. The decline in their number starts from six months and increases depending on the location. The higher the organ is located, the fewer germ cells there are in it. The first sharp decrease occurs by-the 18th month of life, and by the age of 2, about 40% of undescended testicles do not contain spermatogenesis cells. At the age of 3 years, almost 70% of dystopied testicles completely lack sperm formation, and after reachingadulthood — in 100% of cases [7,8]. Unilateral cryptorchidism causes damage in the contralateral testicle and creates conditions for its underdevelopment. A decrease in fertility is observed in 76% of men with a unilateral process. With bilateral abdominal localization, only 4.1% of adult patients have spermatozoa [1,9,]. The anomaly of testicular sinking and differentiation is often considered as an isolated pathological process due to hormonal andanatomomechanical disorders [2]. It was revealed that among the main phenotypic features of the majority of children (92%) with this pathology, there was an asthenic physique. Calculation of the Varge mass-growth index indicated the presence of a body mass deficit (67%). The skin of the patients was thin and easily stretchable (53%), dolichostenomelia was noted (25%). The morphological picture of inguinal canal tissues was characterized by a significant increase in young forms of fibroblasts, mast cells with accumulation of glycosaminoglycan granules. Fiber destruction and lysis were determined in intercellular structures. Subendothelial edema, hemorrhage, and vascular plethora indicated a violation of the microcirculation channel [1]. Microlithiasis in testicular tissue was detected in 10.2% of patients with cryptorchism[2]. It is known that among non-operated children testicular atrophy occurs in 10-15% of cases, hypoplasia-in 40-60%, malignant degeneration of the organ-up to 20%. With a bilateral process, infertility is detected in 70% of cases. Hydrocele, torsion, and cancer of undescended testis are also common complications of cryptorchidism testis[2,4]. The risk of developing malignant degeneration in patients with cryptorchidism is 10 times higher than in men in the general population. Of all those identified by Semin, half are diagnosed in undescended testicles, especially often with an intra-abdominal location. In addition to semen, in men with cryptorchidism. theincidence of chorionicepitheliomas and teratoblastomas is high [1, 5]. Long-term results of surgical treatment show that infertility develops in 50-60% of patients operated on for the disease at the age of more than 5 years. When located in the inguinal canal and especially in the abdominal cavity, testis are exposed to prolonged exposure to high temperature, to which the cells of the spermatogenic epithelium are very sensitive. When histological examination of organ tissue with untreated cryptorchidism, changes are detected as early-as the 1st year of life, and by the age of 4, extensive deposits of collagen are noted in the testicles. At 6 years of age, the pathology is even more noticeable, since the seminal tubules are narrowed, the number of spermatogonia is reduced, and pronounced fibrosis forms around the tubules. At the end of sexual development, the testicles can retain their normal size, but most of the spermatogenic epithelium is absent, so patientsusually suffer from infertility [8]. Since cryptorchidism is an interdisciplinary problem that affects a wide range of specialists (surgeons, pediatricians, endocrinologists), a large percentage of late referral of children for surgical treatment is associated with untimely diagnosis and lack of professional training at the outpatient stage.

Diagnostics. The method of examination and examination of the patient is chosen depending on the age. Newborns and infants are examined in the supine position. Older children can be

examined standing cross-legged. During the study, the inguinal, femoral, pubic areas, perineum, and the opposite half of the scrotum are evaluated. If a testicle is found in the inguinal canal, move it in the direction of the scrotum. In the case when it is possible to lower the testicle into the scrotum cavity, it is necessary to try to fix it there, moderately pressing the edge of the palm on the spermatic cord in order to suppress the cremasteric reflex — this allows you to differentiate between true and false forms of cryptorchidism. Movements during palpation should be gliding, smooth, they should be directed from top to bottom, from outside to inside, along the inguinal canal from the anterior-upper spine of the iliac crest to the scrotum [2,5,5]. The retractile testicle (false cryptorchidism) is normally lowered, but it rises up due to increased reflex activityof the cremaster muscle. Signs of a retractile testicle: when the child is relaxed (especially in a warm bath), the testicle is located in the scrotum; the testicle can be lowered into the scrotum, while it can remain there for some time without tension; half of the scrotum on the test side is well developed. In this situation, several examinations conducted sequentially with an interval of 2-3 months will help to avoid surgical intervention: the testicle will spontaneously fall to its normal place [2]. To determine the localization of the testicles, ultrasound, computed tomography, and scintigraphy are used. Among the hardware methods, ultrasound is the most accessible, the reliability of which with palpable testis reaches 88%. The absence of testis in the inguinal canals, with the exception of ectopia of the organ, will indicate a "syndrome of non-palpable testicles". It causes the greatest diagnostic difficulties, and the localization of the organ cannot be determined in the preoperative period [4]. Diagnostic laparoscopy is currently the only method of investigation that allows you to confirm or exclude the intra-abdominal or inguinal location of the testicles, establish their anatomical characteristics, and make a diagnosis of a missing testicle (monarchism) or testicles (anarchism) [3,5,]. The study of the level of follicle-stimulating, luteinizing hormones and testosterone does not help to clarify the pathology in prepubescent individuals.

Treatment and its results. The first attempts to treat cryptorchidism in children were made by J. Rosenmerkel and M. von Chelius in 2018s. However, only in 2018 T. Annandale performed a successful testicular removal operation in a3-year-old patient [6]. The optimal age for starting treatment (conservative or operative) is 6 months, and this process should be completed by the age of 2 years of the child's life [7]. In some cases, they resort to hormone therapy, which is prescribed jointly by a pediatric surgeon and an endocrinologist. Chorionic gonadotropin (hCG) is used, much less often —gonadotropin-releasing hormone (GnRH), but the effectiveness of this therapy does not exceed 15% and depends on the height of the testicle in the inguinal canal. The more distally the testicle is located in the inguinal canal, the more effective the therapy is. Apparently, higher rates of successful treatment are determined in patients with retracted testicles, which respond well to treatment. HCG is recommended to be used according to the scheme of 3000-10000 IU, the frequency of administration: 1 injection per week for a month, if treatment is ineffective, it is allowed to repeat the course at intervals of 3 months. GnRH is used as a nasal spray at a dose of 1.2 mg /day for 1 month. If conservative therapy is ineffective, surgical treatment is indicated [8,9]. There are about 250 methods of surgical treatment of cryptorchidism, including modifications. Over time, the nature of operational tactics has changed significantly, and new, more gentle methods have replaced traumatic interventions [9]. It is generally accepted that the main stage of surgical treatment of cryptorchidism is various options for fixing the gonads. However, with orchipexia, traction for the elements of the spermatic cord is unacceptable. This causes a reflex spasm of the artery and veins of the organ, and leads to irreversible changesin the germinal epithelium [4]. Testicular removal surgery should be performed by a qualified pediatric uroandrologist or pediatric surgeon. The choice of surgical treatment depends on the form of cryptorchidism.

For inguinal forms Petriwalsky, the Petriwalsky–Shoemaker operation, which was developed in 1929, is indicated. 2 For abdominal forms, one– stage or two-stage laparoscopic reduction according to Fowler-Stephens is preferred. The Petriwalsky-Shoemaker operation for inguinal cryptorchidism is performed from an oblique-transverse incision along the inguinal fold up to 3 cm long. In the inguinal canal, the vaginal process of the peritoneum is isolated, the testicle and spermatic cord are mobilized. It is important to carefully perform orchid funiculolysis with the release of the spermatic cord elements from the cremaster muscle fibers, adhesions, all the way to the inner inguinal ring. With the index finger, a tunnel is formed in the scrotum, the testicle is fixed over the edge of the tunica albuginea to the tunica dartos. The wound on the scrotum is sutured with separate nodal sutures, and the operation is completed in the groin area by applying a cosmetic suture using a self-absorbing material. The efficiency of the Petriwalsky–Shoemaker operation reaches 90% [8].

A. Bianchi and B. R. Squire (2019) proposed to remove the testicle from a single transcrotal approach [4]. The small length of the inguinal canal and the high elasticity of the surrounding tissues make it possible, without opening the latter,to perform a high ligation and cut off the non-obliterated vaginal process of the peritoneum from the oblique-transverse access at the border мof the scrotum and inguinal region [1]. The failures of this method are related to the fact that the short testicular vascular bundle does not allow the testicle to be adequately lowered into the scrotum, as a result of which acute ischemic disorders develop in the postoperative period; they lead to gonadal atrophy in 30-70% of cases. As an alternative to such a one-stage operation for abdominal cryptorchidism, a number of authors suggest microsurgical testicular autotransplantation on the vascular pedicle. The technique is not widely used due to the complexity of implementation. The experience of using it is limited to single observations, and the first resultsare unsatisfactory.

N. Cortesi et al. [2] first described the use of laparoscopic access in the treatment of abdominal formsof cryptorchidism in 201.6.This method allows us to determine the exact location of the "non-palpable" testicle, the condition and length ofsevered arteries and veins. In 2017, based on diagnostic laparoscopy, F. Elanany etal. [3] proposed a 5--stage diagnostic classification of testicular localization and its structures and developed an algorithm for choosing treatment tactics in children with non-palpable testicular syndrome [4]. Known laparoscopic two-stage operation Fowler-Stephens, which is performed with bilateral cryptorchidism with abdominal forms of retention and insufficient vascular length. At the first stage of treatment, the main vascular bundle of the testicle is crossed and the organ is left for 4-6 months to feed at the expense of the pool of a. ductus deferentis and its collaterals, as well as a. cremasterica. After 6 months, the second stageof treatment is performed laparoscopic testicular reduction [5]. During the second stage, the parietal peritoneum and vas deferens are cut out in a single triangular flap on a wide leg, which allows you to cover the ductus deferens and create additional collaterals. Next, a new channel is created to lower the testicle between the medial and median umbilical folds, lateral to the bladder. A transcrotal incision is made. A clamp is inserted into the scrotum cavity, a blunt channel is formed between the skin and the fleshy shell, and the testicle is lowered. Testicle condition is monitored by ultrasound 1, 3, 7 days after surgery. Some authors use a single-stage laparoscopic technique for lowering and fixing the testicle in abdominal cryptorchidism [7]. The advantages of this surgical approach are proven by favorable outcomes [4]. For suturing the peritoneal defect at the level of the inner inguinal ring in the abdominal form of cryptorchidism under video control, a device is proposed that reduces the duration and reduces the trauma of the final stage of the operation [6]. After laparoscopic intervention, patients are discharged home on the 3rd-and-5th days. Wounds are treated with an antiseptic solution, and bathing in the bathroom is excluded for 7days.

A month after discharge, children are necessarily consulted by a pediatric urologist-andrologist and endocrinologist. Testis ultrasound monitoring is performed on an outpatient basis 1, 3 months after surgery. All patients are recommended to have an annual ultrasound screening of the genitals with a mandatory assessment of blood flow in them, monitoring of the hormonal profile during prepubertal and puberty [10]. A comparative study of the immediate and long-term results of treatment of children with abdominal cryptorchidism found that positive outcomes were observed in the group of patients who underwent single-stage laparoscopic orchipexy. In this cohortмес, no testicular hypoplasia was observed 12 months after surgery, and testis volume, resistance index, peak systolic velocity, and end-diastolic velocity were normal [8]. According to other authors, a two-stage Fowler–Stephens endoscopic operation. Stephens in the treatment of cryptorchidism in children is accompanied by a more effective restoration of testicular arterial blood flow compared to a single-stage one. Doppler sonographic examination of testicular arteries in patients after surgical treatment of cryptorchidism proved to be a highly informative method that allowsevaluating the quality of treatment [9].

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