IV. PEDIATRIC SURGERY

MODIFICATIONS OF THE HORMONAL TABLE IN THE UNDESCENDED TESTICLE

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Abstract

A special role in the descend of the masculine gonad is due to testicular hormones (the inhibition factor of Müller ducts and testosterone). Many authors have been preoccupied of the modifications of the hormonal table and fertility at patients treated formerly of cryptorchidism. This paper work describes the role of the testicular hormones in testicular migration and the modifications which take place in cryptorchidism.

Key words: testicular hormones, testicular migration, fertility, cryptorchidism.

The anomalies of testicular migration have preoccupied doctors from ancient times and they have tried to solve this problem and all its levels of manifestation: biological, psychological, social. Although the testicular descend has been described in the specialty literature for over 200 years and numerous studies have been dedicated to the understanding of the phenomenon, the processes and the factors which cause it are still incompletely elucidated problems.

It is known that a special role in the descend of the masculine gonad is due to testicular hormones (the inhibition factor of Müller ducts and testosterone).

The inhibition factor of Müller ducts

The first event of masculine differentiation is the regression of Müller ducts under the influence of the antimüllerian hormone – AMH (the inhibition factor of Müller ducts).

AMH is a glycoprotein with a molecular weight of 140.000, secreted by the Sertoli cells immediately after the constitution of the testicular cordons. By secreting AMH each testicle determines the regression of the Müller ducts on the same side with its position, without influencing the contralaterally Müller duct, so that, at real hermaphrodites, on the testicular side, the Müller ducts can be absent, while on the ovarian side they are normally developed.

In the case of testicular failure of secreting AMH or of the Müller ducts defect of responding to these, the virilism of the genital organs and of the Wolff ducts is normal, but the organs from the Müller ducts are present (men with uterus and uterine tubes) with the appearance of the syndrome of Müller ducts persistence – a type of masculine pseudohermaphroditism with an autosomal recessive or X-linked recessive transmission.

Testosterone

Testosterone is the 2nd genitalia organizer testicular hormonal factor. At humans the gonadal testosterone secretion starts in the 8th week post conception, at the same time with the appearance of the Leydig cells in the testicular interstitial space. In all the genetic defects of testosterone synthesis the virilism of the genital tract is incomplete (in different degrees, in accordance to the severity of the enzymes defects) there being no doubt as to the major role of this hormone in the determination of sexual dimorphism.

Testosterone synthesis

Testosterone synthesis in Leydig cells approximately 20% of the testicular mass) takes place through the same intermediary reactions as the corticosteroids synthesis. The limited speed stage is the split of the lateral chain of cholesterol and the formation of the pregnenolone (Fig. 1.). Testosterone synthesis starts of the level of the internal membrane of the mitochondria in the presence of P450 cytochrome through cholesterol conversion from the plasma or synthesized by Acetyl CoA in pregnenolone. To get to the enzymatic conversion system cholesterol has to pass through the external mitochondria membrane, this being the slow enzymatic step, limiting the synthesis rate of the steroid and probably regulated through LH (*luteinizing hormone*).

The enzymes realize the conversion of the pregnenolone to testosterone in two different ways.

At human the main way of testosterone formation is through progesterone. Dehydrotestosterone is formed in

the testicle or in the peripheral tissues by the action of a 5α-reductase.

The daily secretion of testosterone (7 mg/day/adult person) predominated over the other 2 testicular hormones (dehydrotestosterone – DHT and androstendione) and that is why it is considered the main androgen hormone although a small part is converted at tissue level with 5α-steroid reductase participation into DHT, which is more active. The plasmatic concentration of testicular hormones is 200-300 ng/dl until puberty and 600-700 ng/dl at adults (testosterone = 590 ng/dl).

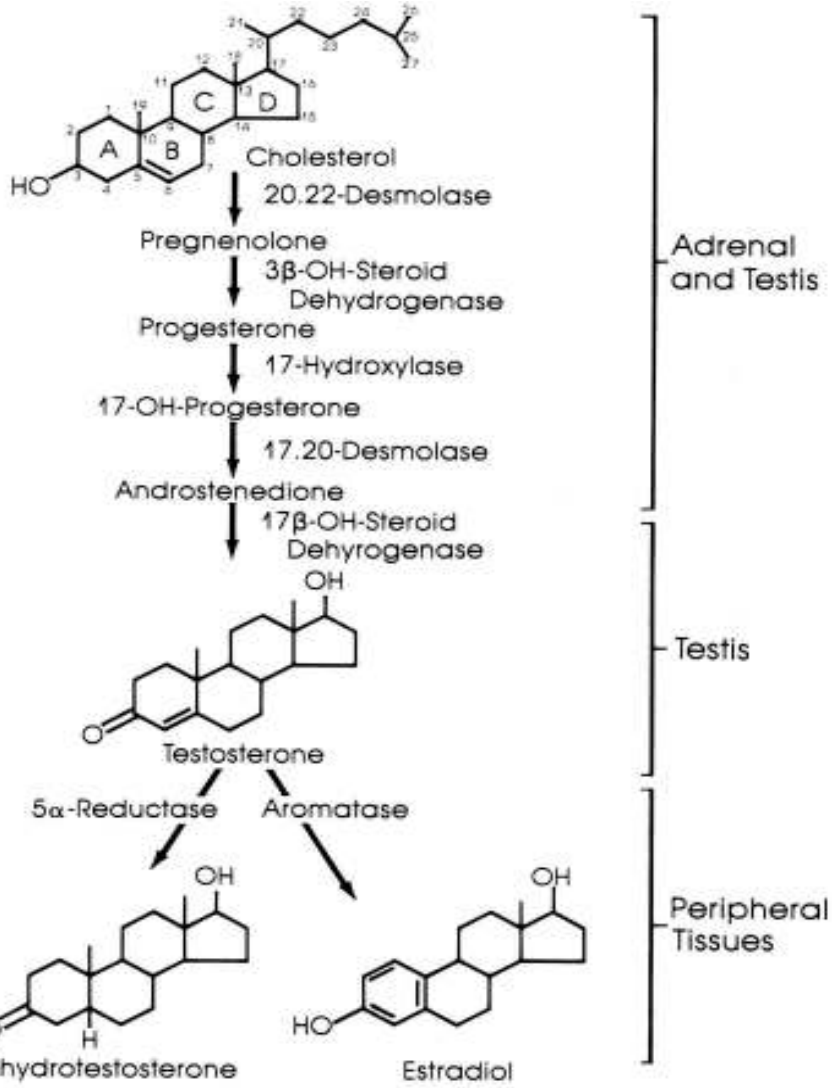

Fig. 1. Androgen synthesis in the testis

Secretion control

The development and the secretion function of the masculine sexual organs are controlled through a mechanism of negative feedback to which the pituitary gonadotropins LH, FSH (*follicle-stimulating hormone*), GnRH (*gonadotropin realising hormone*) and the circulatory testosterone participate.

Unlike spermatogenesis, which depends on the regulatory activity of FSH, the endocrine secretion of the testicles is under the stimulating influence of LH level. This is also called ICSH (interstitial cell stimulating hormone), because it stimulates the interstitial cells described by Leydig. This functions according to the principle of inverse connection establishing relations of positive and negative feedback, with the participation of testicular hormones on one side and the hypothalamic factor which liberates LHRH

(*luteinizing hormone releasing hormone*), on the other side. Hypothalamus represents the final common way at men and women. Although the pituitary secrets 2 gonadotropins, hypothalamus liberates them with the help of a single neurohormon called improperly LHRH. This stimulates LH secretion which, in turn, provokes the hyperplasia of Leydig cells in the testicle and the increased production of testicular hormones from puberty to old age. Testosterone secretion, as the main androgen hormone, is directly proportional to the quantity of circulating LH. Prolactin intensifies the stimulating effect of LH on the production and secretion of testosterone. During gestation placenta releases great quantities of chorionic gonadotropin with a structure almost identical to LH and with a stimulating effect on foetus' Leydig cells, in order to produce the testosterone necessary to the development of the masculine sexual organs.

The excess of circulatory testosterone inhibits the secretion of LH directly and indirectly through LHRH. So testosterone limits its own secretion through its feedback relation to the hypothalamic-pituitary complex. When the concentration of the circulatory testosterone is low, the lack of hypothalamic inhibition leads to its normal secretion (Fig. 2.).

Puberty occurs with the secretion activity of the hypothalamus of LHRH. During childhood hypothalamus does not release factors that start to produce and release LHRH at puberty. LHRH secretion does not appear when the interneuronale connections between hypothalamus and the surrounding nervous formations are not intact. Although the intimate mechanism of puberty is not completely clarified, it seems that this is a process of maturation of the neuronal connections between hypothalamus secreting LHRH and the temporal lobe. The functional unity which exists between the hypothalamus, the pituitary and Leydig cells assures the normal concentration of testosterone in blood, with low daily variations (20-25% higher at 8 o'clock in the morning than at 18 in the afternoon).

At the reciprocal inhibition between the pituitary gonadotropins and the testicular hormones, estradiol participates in a certain degree, as the metabolit of the testosterone.

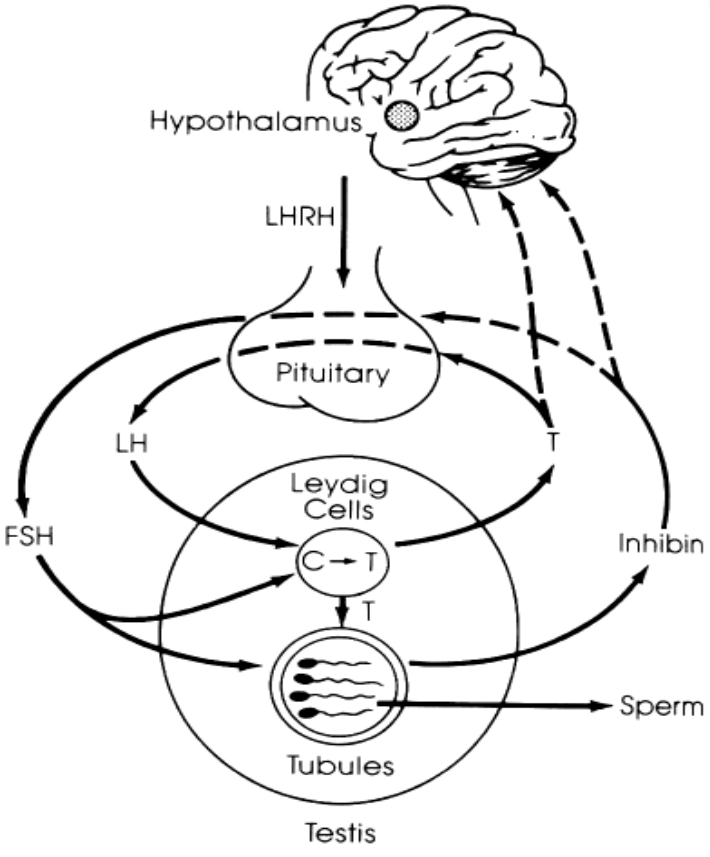

Fig. 2. Regulation of testosterone and sperm production by LH and FSH (C – cholesterol, T – testosterone).

Transport

After its release testosterone is found linked to albumin or a serum globulin for 15-30 minutes.

The hormone is released into blood as it is formed. There are no storage forms. The plasmatic transport is done by a protein which links testosterone and estrogens – SHBG (*sex hormone-binding globulin*) or TEBG (*testosterone-estrogen-binding globulin*). The protein links better to testosterone than to estrogens. SHBG is synthesized by the liver and its production is influenced by a series of factors. The estrogens increase the synthesis of this protein, the thyroid hormones lower it.

Testosterone enters free into the cells and in some tissues it is transformed into dehydrotestosterone. These 2 hormones interact with the same type of intracellular

receptors. The complex hormone-receptor interacts with chromatin and activates the transcription of some genes. The synthesized proteins mediate the biological effects of the hormone. It is not known if all the actions of the testosterone are the expression of a synthesis of all specific proteins.

Action mechanism

After going through the membrane of the target cell, testosterone or its metabolites, resulted from local conversion, exercise their specific action after interacting with nuclear chromatin. In a first phase the steroids are fixed by the specific receptors. Through modifications of the tertiary and quaternary structure of the steroid receptor complex activated complex results, which is fixed at the level of sites of the nuclear membrane and than it is transferred intranuclear. The steroid receptor complex continues to interact, for a limited period, with certain chromatin areas, raising the activity of transcription DNA (*deoxyribonucleic acid*) → RNA (*ribonucleic acid*) and the protein synthesis. In certain tissues (for example the masculine reproductory glands) the interaction of the complex steroid receptor with nuclear chromatin induces DNA and histone synthesis and cells proliferation.

The effects of androgens actions

Androgens are hormones which exercise major influences on the differentiation development and morphofunctional conservation of the genital system and of the sexual characteristics which are secondary masculine, and on the behaviour corresponding to the masculine role in reproduction.

The effects of the action of the testicular steroids on the target organs can be of organization / development or of action. The organizations appear after the exposure at sexual hormones in a critical period of development (usually the prenatal period) and they become permanent, appearing at early stages or only after reaching sexual maturity. The activation effects are the result of the postnatal interaction between gonadal steroids and the target organs and they are reversible and repeatable. A series of organizing effects induced by the sexual hormones prenatal or neonatal manifest themselves at puberty or at adults only in the activating presence of sexual hormones.

Testosterone, together with AMH, cancels the implied tendency of differentiation of the genital system into a feminine one. The androgen makes the genital tract virile, no matter of the genetic sex of the embryo. Each event of the genital differentiation appears after the interaction of the steroid with the target organ in a limited period specific for its development.

At the level of the Wolff duct of the human embryo testosterone conversion in 5α-DHT appears after the 12th week, so after this has become virile. At the urogenital sinus level and the external genital organs 5α-reductase is present before the 6th week. Wolff's ducts virilism would be achieved by testosterone, while the masculine organization of the urogenital sinus and the external genital organs would be the consequence of 5α-DHT action, resulted from the local metabolism of testosterone.

This hypothesis is demonstrated by the fact that, in the deficit of 5α- reductase, individuals, genetically male, with testicles, have external genital organs closer to the fem sex, while the Wolff structures are normally virile.

If the virilism of the urogenital sinus and of the external genital organs are achieved through androgens present in the general circulation, the masculine organization of Wolff duct seems to need higher local testosterone concentrations. When the testicle is unilateral it makes virile completely only the Wolff duct on the same side, the contralateral Wolff duct virilism being absent or rudimentary (as in some cases of real hermaphrodites). The high concentration of testosterone is achieved either from the local diffusion of the hormone or through its secretion in the external ductal system of the testicle.

Testosterone controls the fundamental processes necessary for the development and function of the sexual organs, the appearance and maintenance of the secondary sexual characteristics, spermatogenesis.

Androgens stimulate the protein synthesis, a powerful action at puberty, which leads to the development of bones and skeleton muscles. The effect of the testicle steroids on growth and development of the genital and extragenitale structures at puberty is known (Fig. 3.).

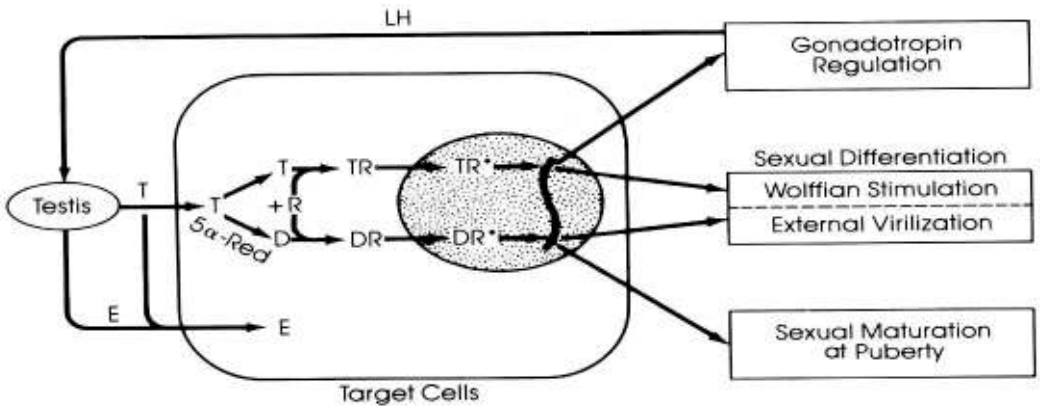

Fig. 3. Current concepts of androgen action (T – testosterone, D – dehydrotestosterone, E – estradiol, R – receptor protein, R* - transformed receptor protein, LH – luteinizing hormone, 5α-Red - 5α-reductase).

Although ovarian estrogens condition the distribution of the fatty tissue and the conformation of the pelvis at women, the major role in determining the sexual and somatic dimorphism at puberty is that of testosterone. The growth of the muscular mass, the modification of the vocal timbre, the growth of the skeleton, hyperpigmentation of the scrotum, the growth of the penis (paradoxically, as during the intrauterine life the phenomenon is mediated by 5α-DHT) are effects conditioned directly by testosterone. It is also the steroid which controls spermatogenesis. The growth in volume of the prostate, acneea, the masculine distribution of facial and body hair, retraction of the temporal hair line are mediated by 5α-DHT.

The endocrine role has been researched with the help of orchiectomy. The consequences of orchiectomy differ, according to age. Before puberty orchiectomy stops the development of the sexual organs and stops the appearance of the secondary characteristics and of the sexual instinct. At adults the effects of orchiectomy are less evident, limited to the involution of the sexual organs and the reduction of virility. The administration of total extracts or androgens hormones eliminates the functional and metabolic consequence of orchiectomy or of the testicular insufficiency both before puberty and at adults.

Testosterone functions are closely linked to the development of the primary and secondary sexual characteristics at man. If during foetal life and in the weeks after birth testosterone secretion is stimulated by chorionic gonadotropin, then the testosterone secretion stops, until puberty, under the influence of the pituitary gonadotropin. After the age of 50 it drops rapidly reaching 20% of its maximum value at the age of 80 (Fig. 4.).

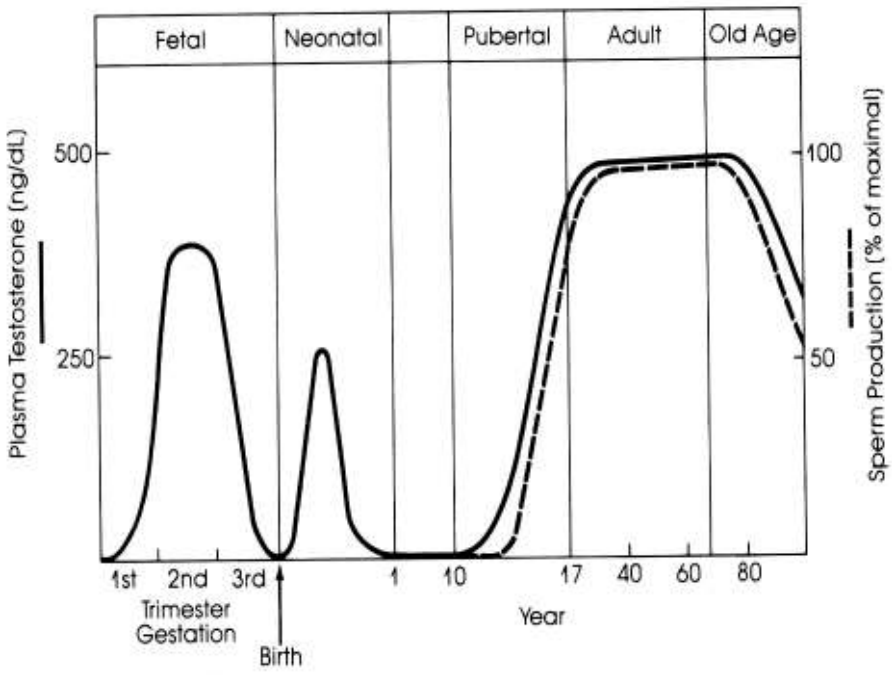

Fig. 4. Testosterone level variation during on the men's life.

During foetal development testosterone helps the growth of the genital organs and the descend of the testicles in scrotum in the last 2 months of gestation. In the case in which the descend did not take place before birth the administration of testosterone or of pituitary gonadotropin will help the descend take place in the days or weeks that follow.

At puberty testosterone secretion stimulates the development of the genital organs until the age of 20 and of the secondary sexual characteristics (pubian hair, chest and facial hair, thickening of voice and skin, development of the muscles of the skeleton). The cutaneous stimulating properties seldom determine the appearance of acneea at puberty.

The biological effects of the testicular hormones can be classified according to the place and way of action in androgenic and anabolic effects.

In turn the androgenic effects are partially defined in the case of testosterone and dehydrotestosterone both in the foetal period and also at puberty. While testosterone stimulates, in the fetal period, the differentiated development of epididim, deferent ducts and seminal vesicles dehydrotestosterone assures the formation of the penis, urethra, scrotum and prostate. During puberty

testosterone stimulates especially the spermatogenesis and the development of the penis, the seminal vesicles, the larynx and the muscles of the skeleton, while dehydrotestosterone has an action on the prostate, the scrotum and the secretion of the prostate. On a behavioural level testosterone stimulates potency and libido. At adults the androgens effects of the both testicular hormones have as consequences baldness, skin thickening and contain particularities of anabolic effects.

Anabolic effects assure growth, maturity and puberty virilism in general, as a consequence of activating the protein synthesis and the phosphor and calcium metabolism at the level of different tissues and organs (skeleton muscles, bone matrix, bone marrow, and nervous tissue) and especially of those involved in the reproduction function. At the cellular level testicular hormones are fixed on a common receptor which moves them in the nucleus to action upon a chromosomal DNA stimulating RNA-polymerase and the formation of RNA as the main place of protein synthesis. Through such a mechanism of intensifying the protein synthesis, the growth of muscular mass during puberty is achieved and the anabolic effects of the testicular hormones at adults and old people, improving vigour and muscular force. Testicular hormones have an action of intensification of osteosynthesis and growth in length of the bones during puberty, as a consequence of bone matter growth. At the same time with bone thickening, in the post puberty period, the ossification of the growth cartilage and the stop of stature development are produced. At adults testosterone provokes sodium and water retention trough the mechanism of activating the processes of tubular resorption. The high quantities of testosterone lead to the growth of basal metabolism and of the number of red blood cells with 10-20%.

Metabolism

At the level of the peripheral structures testosterone is metabolized, being a prohormone for a series of other steroids. Depending on the target tissue testosterone is converted into more active androgens, estrogens or steroids without action on the genital system. As a consequence testosterone effects (or other androgens) are specific for certain organs (different for diverse organs).

One of the important ways of testosterone metabolism is the conversion to 5α-DHT at the level of genital organs, skin and brain. The androgen effect of 5α-DHT on the genital organs is 2,5 more powerful than testosterone.

At adults the daily production of 5α-DHT is 300-400 μg, and the plasmatic 5α-DHT/T rapport is 1/10 at men and 1/3-1/4 at women.

The metabolites of the 5ß-testosterone, resulted trough the conversion of the hormone at the level of liver or bone marrow, are responsible of the anabolic action of the androgens at the level of these organs.

Testosterone is also a major prohormone for the circulatory estrogens. At man 20% of the daily synthesis of estradiol (65μg for a healthy adult) is of testicular origin, the rest resulting from the peripheral metabolism of testosterone.

Metabolites are eliminated in the urine. Women's urine also contains metabolites of androgen hormones which are produced by the ovaries and from adrenal cortex. Men's urine also contains estrogens, secreted by Sertoli and Leydig cells as metabolic products which come from testosterone. Only 20% of the urinary corticosteroids come from testicular testosterone.

Approximately 1% of testosterone is eliminated as testosterone-17 and androstendione-glucuronid (these steroids come from the testicular testosterone).

Modifications of the hormonal table in the undescended testicle

Because of the implications of the hormonal placenta dysfunctions or hypothalamic dysfunctions in the aetiology of testicular migrations disorders as well as of the possible role of hypogonadism along a raise in temperature, the study of the serum values of gonadotropins and testosterone in diseases were of a real interest.

During prepuberty the low serum levels of these hormones make it difficult to determine the basal hormonal values. With the debut of puberty the basal values of gonadotropins and testosterone, and those resulted after stimulation, increase quickly.

The postnatal testosterone increase is at the normal superior limit at newborns with cryptorchidism, at whom the testicle descends spontaneously in the scrotum in the first 4 months and is low or absent at those without descended testicles and after 120 days the differences between the two groups disappear. At a serum testosterone level > 3 ng/ml all testicles descend.

The post natal testosterone increase is correlated positively to the LH serum levels, gonadotropins values being low at those with untreated cryptorchidism, FSH level being identical at the two groups (treated or not) and the serum levels of testosterone and gonadotropins are similar in bilateral and unilateral cryptorchidism.

Many authors have been preoccupied of the modifications of the hormonal table and fertility at patients treated formerly of cryptorchidism. Although there are many contradictory opinions, I'll present the most important studies in a chronological order.

Scheiber K and collaborators determined testicular volumes and exocrine testicular function in 82 men who had undergone orchidopexy (36 bilateral, 46 unilateral) at 5-18 years of age in 1981. The testicular volumes at patients with unilateral and bilateral orchidopexy correspond to those on normal mature males. Semen analyses in unilateral cryptorchidism were normal in 13, doubtful in 23 and pathological in 10 patients. Out of a total of 36 patients who have undergone bilateral orchidopexy, 3 patients were found to have normal, 7 patients doubtful and 26 patients' pathological sperm analyses. Endocrine evaluation in bilateral cryptorchidism (at pre puberty, puberty and post puberty) showed no differences in testosterone levels compared to control groups. Some post puberty patients with pathological sperm analyses were

found to have elevated LH and FSH levels; 22 post puberty patients with pathological sperm analyses showed hypergonadotropism with markedly elevated LH and FSH levels after GnRH.

Kawada T and collaborators measured immunoreactive inhibin, FSH, LH, and testosterone in 17 patients after orchidopexy in 1995. FSH was extremely high (20 mIU/ml or above) in 3 patients. The inhibin level was significantly lower in these 3 patients than in the other 14 patients. All 3 high-FSH patients had azoospermia. Testosterone and LH were normal in one of them. Even considering problems involved in the inhibin assay, the high FSH levels are considered to reflect reductions in the blood inhibin level due to Sertoli cell dysfunction. These findings suggest that inhibin plays an important role in the suppression of FSH at least in some patients after orchidopexy.

Taskinen and collaborators evaluated the effect of patient age at treatment of cryptorchidism in relation to subsequent semen quality in 1996. Semen analyses and hormonal evaluations were performed in 51 men who were treated for cryptorchidism at ages 10 months to 12 years. Sperm concentration was normal in 90% of the patients with unilateral and 50% with bilateral cryptorchidism. No patient treated before age 4 years had severe sperm defects. Elevated follicle-stimulating hormone levels indicated severe testicular damage. Fertility was better in patients with bilateral cryptorchidism if treated before age 4 years. Age at treatment did not have a significant effect on semen quality in patients with unilateral cryptorchidism.

In 1997 Lenzi A and collaborators studied 71 patients with unilateral cryptorchidism who underwent orchidopexy in prepubertal age (6.4 +/- 2.8 years), followed up as adults (20.0 +/- 2.8 years). Patients underwent testicular examination and hormonal evaluation, 49 of these had semen analysis and antisperm antibody tests. Semen results were compared with those of two age-matched control groups: a group of 20 healthy, randomly selected subjects and a group of 20 patients operated on in postpubertal age for cryptorchidism. Unilateral reduced testis size was found in 30.1% of patients, eight patients had a low LH level, eight had a low T level, and none had abnormal FSH values. Antisperm antibodies were found in 1 of 49 cases. Cluster analysis of sperm parameters showed that the mean values of patients were worse than those of the healthy controls but better than those of the subjects operated on in postpubertal age. This study indicates that prepubertal orchidopexy can give better results than postpubertal correction.

Crespo Chozas and collaborators studied 20 postpubertal males with a mean age of 17.35 years (range: 15-21 years) and treated for cryptorchidism during childhood were evaluated for pubertal development and gonadal function in 1999. A hormonal study which included basal determinations of testosterone, luteinizing hormone (LH) and follicle-stimulating hormone (FSH), and semen analysis was performed on each patient. Complete virilism was observed in all patients. The start and development of puberty were normal in all cases (except one patient that started puberty at 10 years of age). Basal studies in all patients showed normal levels of LH and testosterone. FSH levels were increased in 3 patients and normal in the other 17 patients. Fourteen patients achieved normal spermatogenesis with more than 20 million spermatozoids/ml. In the other 7 patients (35%), 5 with unilateral cryptorchidism and 2 with bilateral cryptorchidism, the sperm count remained below 20 million with a range of 0.8 to 18.4 x 10^6 spermatozoids/ml. The three males with elevated levels of FSH also presented oligospermia. The results showed that pubertal development is normal after cryptorchidism. Impaired spermatogenesis was a major factor in undescended testes. Basal FSH levels can be useful in predicting germinal damage secondary to cryptorchidism.

Lee PA and collaborators studied 84 men with a history of unilateral cryptorchidism in 1999. They found that age at orchidopexy significantly correlated inversely with inhibin B and positively correlated with FSH. Comparison of mean hormone levels and sperm density by analysis of variance for linear trend revealed a significant relationship between age at surgery with inhibin B and testosterone, while sperm density, FSH and luteinizing hormone were not significantly related. Men who previously had unilateral cryptorchidism and who underwent orchidopexy by age 2 years have higher inhibin B and lower FSH profiles than those who underwent surgery later in life. This finding suggests an overall beneficial effect of early orchidopexy in boys born with unilateral cryptorchidism.

The same authors compared sperm counts and gonadotropin levels before and after gonadotropin-releasing hormone stimulation between formerly unilaterally cryptorchid men and controls that had completed a detailed questionnaire on fertility and other pertinent paternity information. These parameters were also compared between the subsets of formerly cryptorchid men who reported paternity and unsuccessful attempts at paternity. Sperm density and total count, and basal and gonadotropin-releasing hormone stimulated follicle-stimulating hormone (FSH) levels were different in the cryptorchidism and control groups. Higher FSH levels and lower sperm counts correlated inversely in the cryptorchidism group, while luteinizing hormone, testosterone and other results of semen analysis did not differ. Furthermore, FSH levels were higher and sperm counts were lower in the subset who reported unsuccessful attempts at paternity compared with those reporting paternity. Other measured parameters did not differ between these groups. They concluded that FSH levels are significantly higher and sperm counts are significantly lower in formerly cryptorchid men than in controls. In the cryptorchidism group the same differences are found in fertile and infertile men. Thus, elevated FSH and low sperm counts may be considered risks for infertility in formerly cryptorchid men.

In 2000, the same authors, determined differences in paternity and levels of the hormones inhibin B, follicle-stimulating hormone, luteinizing hormone, testosterone and free testosterone based on the preoperative location of the undescended testis in men with previous unilateral cryptorchidism. In 103 cases they performed semen

analysis and measured the levels of the hormones inhibin B, luteinizing hormone, follicle-stimulating hormone, testosterone and free testosterone. Paternity, sperm count and hormonal parameters were compared with cryptorchid testicular location. Logistic regression was done to analyze pre-treatment testicular location as a risk factor for infertility. Paternity, duration of attempted conception in men who achieved paternity, sperm count and hormone levels did not differ based on abdominal, internal ring, inguinal canal, external ring, upper scrotum or ectopic testicular location. The overall paternity rate was 90% with the lowest rate of 83.3% in the abdominal group. More than 12 months were required to achieve conception in 28.9% of the study group overall and in 39.4% of the abdominal group. Varicocele and a partner with fertility problems were risk factors for infertility, while abdominal testicular location caused borderline significant risk. They concluded that preoperative testicular location in men with previous unilateral cryptorchidism is not a major determinant of fertility according to paternity, sperm count or hormone levels.

In 2001, in Italy, Vinardi S and collaborators evaluated testicular volume, serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone as well as semen specimens, in 57 men (mean age, 19 years; range, 18 to 27 years) treated in childhood for unilateral (n = 47) and bilateral (n = 10) cryptorchidism. In 3 unilateral cases monorchidism was found. Thirty-seven patients underwent orchidopexy after hormonal treatment (luteinizing hormone releasing factor, 1.2 mg/d for 28 days followed by human chorionic gonadotropin, 500 IU intramuscularly 3 times a week for 3 weeks). The remainder underwent surgery. Mean age at surgical treatment was 5.4 years (range, 2 to 12 years). These patients were examinated again after a mean period of 13.3 years (range, 10 to 19 years). Reduced testicular volume (<12 mL) was found in 6 of 64 testes (9.3%). LH, FSH, and testosterone levels were found within the normal range in all patients. With linear regression, inverse relations were found between FSH and, respectively, testicular volume, sperm concentration, sperm motility, and normally shaped sperms. There were direct relations between testicular volume and sperm concentration, sperm motility, and normally shaped sperms. They did not find any statistical correlation between age at surgery and semen quality. Significantly better results in terms of sperm counts were found in patients directly operated on in comparison to those treated with hormones before orchidopexy.

Cortes D and collaborators studied 135 patients with cryptorchidism (70 bilateral and 65 unilateral) in 2003, who had a simultaneous biopsy taken at orchidopexy in childhood, and in adulthood had analyses of semen and FSH. In adulthood 42 formerly bilateral cryptorchid boys had repeat testicular biopsies taken. Infertility was suspected in men with < 5 million sperm/mL in the best sample of semen and concomitant poor sperm motility, and who were classified by follicle-stimulating hormone (FSH) values. At orchidopexy the number of spermatogonia/tubule and the germ cell differentiation were measured. In adulthood the percentage of tubules with complete spermatogenesis, spermatogenic arrest and Sertoli-cell only status was assessed. Infertility was suspected in 38 of 70 (54%) of formerly bilateral and six of 65 (9%) formerly unilateral cryptorchid patients. High FSH values were expected in these suspected infertile patients, but 15 of 38 (59%) formerly bilateral and five of six formerly unilateral cryptorchid patients had normal FSH values. These patients were identified in childhood at orchidopexy; those with bilateral cryptorchidism generally presented with germ cells, but the mean number of spermatogonia per tubule was < 30% of the lowest normal value, and the germ cells were seldom normally differentiated, whereas those with unilateral cryptorchidism generally lacked germ cells in the biopsies. No patients had a decreased FSH value.

By analyzing these studies the conclusion is that the level of testosterone and LH, in the majority of the cases of undescended testicle, is in normal limits, while FSH levels modifies in connection to fertility. So, while oligospermia is high, FSH values are high too. The infertility rate is 50% in some studies, when the disease is bilateral and 10% when it is unilateral. There are no major influences regarding the initial position of the undescended testicle, but the best results were obtained in the case of orchidopexy until the age of 2 years.

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