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Testicular neoplasia in undescended testes of cryptorchid boys-does surgical strategy have an impact on the risk of invasive testicular neoplasia?

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SUMMARY: Cortes D, Thorup J, Petersen BL. Testicular neoplasia in undescended testes of cryptorchid boys-does surgical strategy have an impact on the risk of invasive testicular neoplasia? Turk J Pediatr 2004; 46 (supplement): 35-42.

We investigated whether or not surgical strategy has an impact on the risk of invasive testicular neoplasia in cases of cryptorchidism.

We made a database study of the incidence of testicular neoplasia at surgery for cryptorchidism in childhood, and evaluated if such abnormalities were found in special categories of patients, and also of the incidence of testicular neoplasia after orchiopexy with a simultaneous testicular biopsy in childhood.

At surgery for cryptorchidism the risk of testicular neoplasia was 7/182 (4%) in cases with intra-abdominal testis, abnormal external genitalia other than cryptorchidism, or diagnosed abnormal karyotype, versus no case in the 1281 patients without these characteristics (Fisher's exact test, $p<0.00005$). These clinical characteristics occurred most often in bilateral cryptorchidism 82/339 (24%) versus 103/1127 (9%) in unilateral cryptorchidism (Fisher's exact test, $p<0.00005$). At follow-up, the risk of testicular neoplasia was 7/830 (1%). The relative risk of testicular neoplasia was about 4.

Conclusion: Based on our data and the literature we recommend: 1) Taking a testicular biopsy at surgery for cryptorchidism in childhood in intra-abdominally placed testes, or if the patient has abnormal external genitalia or a known abnormal karyotype. These clinical characteristics occur most often in cases of bilateral cryptorchidism. 2) Surgery for cryptorchidism before 10 years of age 3) Clinical control, after surgery for cryptorchidism. In cases of testicular atrophy orchiectomy must be considered.

***Key words:** cryptorchidism, carcinoma-in-situ-testis, seminoma, abnorml external genitalia, abnormal sex chromosomes, intra-abdominal testis.*

Cryptorchidism is associated with testicular cancer. On the basis of mixed groups of men treated for cryptorchidism the risk is stated to be 3.6 to 7.4 times higher than in the general population[1-6]. Around 1995, the incidence of testicular cancer in Denmark was approximately 10 per 100,000 men. It is among the highest registered incidences in the world, with a lifetime risk of testicular cancer of 0.5-0.7% for Danish men in the general population against 2-3% in men treated for cryptorchidism[4,6]. Although cryptorchidism is associated with testicular cancer, only about 5% of these cases can statistically be referred to cryptorchidism[6].

Increasing incidence rates of testicular cancer have been found in many populations of European origin[6]. The reasons for this is not known. Testicular cancer occurs in infants, with a small peak incidence, but less than 1% of testicular cancers occurs before 10 years of age. The incidence curve increases steeply after the onset of puberty and is most frequent in men in their 20s and 30s; 50% are diagnosed before the age of 35 years. In Denmark, testicular cancer is the most frequent malignancy in young men. In the age interval 10-59 years, more than 95% of testicular cancers are germ cell cancers[6].

At time of surgery for cryptorchidism in childhood, testicular neoplasia has been described[7]. This neoplasia may be an invasive germ cell tumor, or it may be a premalignant condition named carcinoma-in-situ-testis, which

was reported first in 1984 in an undescended testis. The history for such a condition was not known at that time. Consequently, the 10-year-old patient with carcinoma-in-situ-testis was followed with repeated testicular biopsies, and after 11 years invasive testicular neoplasia was found, confirming that carcinoma-in-situ-testis is a premalignant pattern in undescended testes of boys as well[8]. The transformation from carcinoma-in-situ-testis to invasive cancer may depend on male sex hormones, as testicular cancer very rarely develops in absence of these hormones[4,6,9].

Based on our data, and the literature, we will focus on the possibilities for surgery to avoid development of invasive testicular cancer in cases of cryptorchidism.

Material and Methods

The study includes 1,466 consecutive cryptorchid boys who underwent surgery for cryptorchidism with simultaneous testicular biopsy between January 1971 and 1 March 2004. Testicular parenchyma was demonstrated in a total of 1805 specimens. All the case reports were reviewed. Previous reports described 1026 of the biopsies in detail[10,11]. The age of patient at surgery, testicular location and associated abnormalities were taken from case reports. Excluded were patients with fallopian tubes or a uterus, and patients who had developed cryptorchidism after surgery for an inguinal hernia. All tissue specimens were fixed in Stieve's solution, embedded in paraffin, and 4 μ-sections were stained with hematoxylin-eosin and van Gieson's staining. From April 1997 the majority of sections underwent further staining with anti-MIC-2[12].

We investigated if testicular neoplasia was present in these biopsies taken simultaneously at surgery for cryptorchidism. Furthermore, we evaluated if testicular neoplasia was associated with bilateral cryptorchidism, an intra-abdominal testicular position, abnormal external genitalia other than cryptorchidism, or known abnormal karyotype.

In addition, to explore the risk of testicular cancer in an unselected population of biopsied undescended testes, we investigated a cohort of 830 men who had orchiopexy of 1026 undescended testes between January 1, 1971 and January 1, 1992, and who were aged at least 18 years at August 31, 1992. Information on cancer occurrence, including date of diagnosis and tumor type, were obtained from the Danish Cancer Registry on December 31, 1994. The Danish Cancer Registry records all cases of cancer in the Danish population. A previous report has described the patients and method in detail[10,11].

Moreover, we studied in the literature whether or not certain treatment modalities reduce or increase the risk of testicular cancer in cases of cryptorchidism.

Results

Table I shows the total occurrence of testicular neoplasia at surgery for cryptorchidism. There was one case of invasive germ cell tumor, six cases of testicular carcinoma in situ, and one Sertoli cell tumor. Five cases of testicular neoplasia were determined in patients who had undergone bilateral surgery for cryptorchidism and in whom bilateral testicular parenchyma was demonstrated at time of surgery. Consequently, the risk of testicular neoplasia was 5/339 in these cases, 1.5%, which was significantly higher than the risk of testicular neoplasia among the patients with unilateral surgery for cryptorchidism and unilateral biopsy demonstrating testicular parenchyma, 0.2% (2/1127) (Fisher's exact test, $P<0.05$).

However, testicular neoplasia was demonstrated in cases of unilateral cryptorchidism. These two patients, unlike the majority of unilateral cryptorchid patients, had intra-abdominal testis (case 2) and abnormal karyotype (case 7). In total, of the eight testes with neoplasia from seven patients, three neoplasms were diagnosed in intra-abdominal testes (cases 1-3), four occurred in three boys with abnorml external genitalia other than cryptorchidism (cases 4-7), and two were diagnosed in boys with known abnormal karyotype (cases 3 and 7). Analysis of the risk of testicular neoplasia associated with each of these characteristics was complicated by the fact that some patients had more than one of the characteristics. Among the 131 boys (145 specimens) with intra-abdominal testes, four had known abnormal karyotype: 46,XY/47,XYY (case 3), 46,XYdel(11p), 46,XY,13/20 unbalanced translocation and 46,XY/45,XO, the latter furthermore had hypospadias and bifid scrotum. In addition, five of the patients with

Table I. The Occurrence of Testicular Neoplasia in Eight Undescended Testes From Seven Cryptorchid Boys, Among 1466 Patients Who at Median Age 11.4 Years (Range 0.1-18.9 Years) Underwent Surgery for Crytorchidism, with Examination of 1807 Specimens of Testicular Tissue from Undescended Testes

Case No.	Age at surgery for cryptorchidism (years)	Anatomical position of the testes	Record of testicular neoplasia and findings in the contralateral testis	Characteristics
1	13.3 (right) 13.3 (left)	Intra-abdominal Intra-abdominal	Germ cell hypoplasia Carcinoma-in-situ-testis	Intra-abdominal testes, 46,XY, no abnormal genitalia
2	(right) 5.4 (left)	Scrotum Intra-abdominal	The parents wanted no biopsy Carcinoma-in-situ-testis	Intra-abdominal testis, 46,XY, no abnormal genitalia
3	7.1 (right) 7.1 (left)	Intra-abdominal Intra-abdominal	Large cell calcifying Sertoli cell tumor of the testis No germ cells	Intra-abdominal testes, abnormal karyotype: 46,XY/47,XYY. No abnormal external genitalia.
4	10.2 (right) 10.6 (left)	External inguinal ring External inguinal ring	Carcinoma-in-situ-testis Carcinoma-in-situ-testis	Abnormal external genitalia: a small penis, a vaginal pouch and a bifid scrotum, 46,XY[34]
5	10.9 (right) 10.8 (left)	External inguinal ring External inguinal ring	Carcinoma-in-situ-testis Germ cell hypoplasia	Abnormal external genitalia: a small penis and a partially bifid hypoplastic scrotum[10]
6	18.6 (right) 18.6 (left)	Inguinal canal External inguinal ring	Seminoma Germ cell hypoplasia	Abnorml external genitalia: a small penis and a hypoplastic scrotum, 46,XY[10]
7	15.4 (right) 15.4 (left)	Inguinal canal Scrotum*	Carcinoma-in-situ-testis Germ cell hypoplasia	Abnormal karyotype: 45,X/46,XY[10]

The seven cases were published in a table in BMJ[45].
* This biopsy from a scrotal testis was not included in the material of 1807 specimens of testicular tissue from undescended testes.

intra-abdominal testes had abnormal external genitalia, two with hypospadias, one with hypospadias and bifid scrotum, and two with small penis and scrotum. Furthermore, 38 patients (56 specimens) had abnormal external genitalia but no intra-abdominal testes: 18 with hypospadias, three with epispadias, two with some ambiguity of the external genitalia (cases 4 and 5) and one with hypoplastic scrotum, and 14 with small penis and scrotum, of whom five had Kallmann's syndrome, one had testicular neoplasia (case 5), and one in addition had abnormal karyotype 47, XYY. Moreover, 16 patients (22 specimens) had known abnormal karyotype, but neither intra-abdominal testes nor abnormal external genitalia: eight with Klinefelter's syndrome, 47,XXY; three with Prader-Willi syndrome, 46,XYdel(15q)paternal one with 45,X/46,XY (case 7); one with 46,XX/46,X(delY); one with a 46,XY,3/21 balanced translocation; one with 46,XY,3/14 unbalanced translocation and one with 46,XYdel(2p).

In total at surgery for cryptorchidism the risk of testicular neoplasia was 4% (7/185, 95% confidence limits 1.5-8%) in the patients with intra-abdominal testis, abnormal external genitalia other than cryptorchidism, or diagnosed abnormal karyotype. In contrast, no case of testicular neoplasia occurred in 1281 patients without these characteristics. The figures are significantly different (Fisher's exact test, $P<0.00005$).

Intra-abdominal testis, abnormal external genitalia, or abnormal karyotype was reported in 82/339 (24%) of the patients operated for bilateral cryptorchidism, and in whom bilateral testicular parenchyma was identified. This figure was significantly higher than the frequency of these characteristics, 103/1127 (9%), among the patients who had undergone unilateral surgery for cryptorchidism and demonstrated unilateral testicular parenchyma in the specimen (Fisher's exact test, $P<0.00005$).

In the patients with bilateral cryptorchidism and bilateral testicular parenchyma and furthermore intra-abdominal testis, abnormal external genitalia and/or known abnormal karyotype, the

risk of testicular neoplasia was 6% (5/82, 95% confidence limits 2-14%). However, this was not statistically significantly higher than the risk of testicular neoplasia in the group of patients with unilateral cryptorchidism and unilateral testicular parenchyma and furthermore intra-abdominal testis, abnormal external genitalia and/or known abnormal karyotype (2%) (2/103, 95% confidence limits 0.2-7%), (Fisher's exact test, p=0.2793). Consequently, testicular neoplasia is associated with intra-abdominal testis, abnormal external genitalia and/or known abnormal karyotype and not to bilateral cryptorchidism.

In one patient a diagnosis of carcinoma-in-situ-testis was suspected based on the morphology of the germ cells nuclei. However, the PLAP, P53 and CD117 staining were all negative, pointing against the diagnosis of carcinoma-in-situ-testis. The FISH for the X and the Y chromosome in the testicular biopsy showed maximally 1 copy of each, corresponding to a normal male karyotype. The histological specimen furthermore showed a pattern of multinucleated spermatogonia, which may be a premalignant histological pattern[13]. The undescended testis was placed at the external inguinal ring. The patient was 3.8-years-old at surgery for unilateral cryptorchidism and he had no associated anomalies. His parents were informed about the concern regarding the former undescended testis. They choose orchiectomy, as the contralateral testis was normal looking and well in the scrotum. Orchiectomy has not yet been performed for the possible malignant transformed testis.

In the Danish Cancer Registry, among the 830 patients with a history of orchiopexy, we identified seven cases of testicular neoplasia (Table II). Of the seven cases, one occurred before a biopsy sample was taken from the contralateral testis (case 1), three were diagnosed by histological examination at the time of surgery for cryptorchidism (cases 2-4), two occurred in previously biopsied testes (cases 5 and 7), and one was a contralateral cancer in a man previously operated for unilateral cryptorchidism (case 6). Histological examination at the time of surgery for cryptorchidism revealed one case of seminoma and two cases of carcinoma in testes (cases 2-4). If these three cases had become clinically manifest as invasive cancer later the number of cases during follow-up would have been six and the relative risk would have been about four-fold, which is the rate expected in a population of men treated for cryptorchidism[11]. In the cohort of 830 men, we found that the three cases of testicular neoplasia that occurred in men who had a testicular biopsy in one or both testes (cases 5-7) corresponded to a relative risk of 2.0 for testicular neoplasia after taking one testicular biopsy at surgery for cryptorchidism in childhood, while the two cases in bilateral

Table II. The Occurrence of Testicular Neoplasia in 830 Men Who Had Testicular Biopsy Samples Taken at Time of Surgical Treatment for Cryptorchidism

Case No.	Age at surgery for cryptorchidism (years)	Record of testicular neoplasia	Diagnosed at time of surgery for cryptorchidism
1	14.3 (right)	Yolk sac tumor in normally descended testis at 1.8 years	No
2	18.6 (right and left)	Seminoma in right testis at 18.6 years	Yes
3	15.4 (right)	Carcinoma-in-situ-testis in right testis at 15.4 years	Yes
4	10.2 (right) 10.6 (left)	Carcinoma-in-situ-testis in right testis at 10.2 years and Carcinoma-in-situ-testis in left testis at 10.6 years	Yes Yes
5	13.6 (right and left)	Non-seminoma in left testis at 27.5 years	No
6	11.3 (right)	Non-seminoma in normally descended left testis at 24.1 years	No
7	14.8 (right and left)	Seminoma in right testis at 36.2 years	No

The seven cases were first published in a table in BMJ[46].

biopsied testes (cases 5 and 7) corresponded to a relative risk of 2.2 (Table II)[11]. It is noteworthy that germ cells were not exhibited in bilateral biopsy specimens obtained at bilateral orchiopexy in the 13-year-old patient who was treated for malignant germ cell tumor at age 27 years (Table II, case 5), or in the biopsy specimen obtained at unilateral orchiopexy in the 11-year-old patient who at age 24 years had a malignant germ cell tumor in the contralateral scrotal testis (Table II, case 6). The other patient (case 7) who was treated for malignant germ cell tumor at age 36 years (Table II, case 7), bilaterally had severe germ cell hypoplasia when he was 14 years old and underwent bilateral orchiopexy.

Discussion

All seven boys with testicular neoplasia at surgery for cryptorchidism had intra-abdominal testis, abnormal external genitalia, or known abnormal karyotype. No case of testicular neoplasia was found in patients without these characteristics. This information is important, and not in conflict with the literature, as carcinoma-in-situ-testis has been reported in four patients, 0.3-15 years of age, with 45,X/46,XY karyotype and cryptorchidism[14,15], and in a 17-year-old boy with ambiguous genitalia, 45,X/46,XY karyotype and Y chromosome microdeletions[16]. Carcinoma-in-situ-testis has also been reported in an intra-abdominal testis of a 13-year-old bilateral cryptorchid boy with small penis, penoscrotal hypospadias and karyotype 46,XY[17]; in intra-abdominal testes of a 13-year-old boy with 46,XY karyotype[18]; in intra-abdominal testes of two boys older than 12 years[19]; in a 17-year-old boy with prune belly syndrome[20]; in an impalpable testicular remnant of a 9-year-old boy[21]; and in an inguinal atrophic testis of a 16-year-old-patient[22].

The presence of carcinoma-in-situ-testis in these patients is consistent with the increased risk of developing testicular germ cell tumors in patients with abnormal karyotype, especially 45,X/XY[15,17,23-25]. Klinefelter's syndrome is especially associated with extragonadal germ cell tumors, but possibly also with testicular germ cell tumor[26,27]. Carcinoma-in-situ-testis has been reported in a 16-week-old fetus with trisomy 21[28], which is consistent with reports of trisomy being associated with germ cell tumors[27,29]. Boys with abnormal external genitalia and normal 46,XY karyotype also have an increased risk of developing testicular germ cell tumors[17,24,25]. Generally, the risk of developing germ cell tumors is reported to be higher in intra-abdominal testes[1], and three out of four germ cell tumors reported in 2918 men who underwent surgery for cryptorchidism and inguinal hernia developed in previously intra-abdominal testes[3]. These four patients had had bilateral intra-abdominal testes at operation when 2, 6, 14 and 15 years old. Karyotype and a possible presence of additional abnormalities were not stated and examination for carcinoma-in-situ-testis was not done at orchiopexy[1,3].

In clinical practice, we recommend a testicular biopsy at surgery for cryptorchidism if the boy has intra-abdominal testis, abnormal external genitalia, or known abnormal karyotype. In our material, 13% (185/1466) of the patients were included in this group. It is important that the risk of intra-abdominal testis, abnormal external genitalia, or known abnormal karyotype was higher in the patients with bilateral than with unilateral cryptorchidism. This is in accordance with a higher risk of testicular neoplasia in the patients with a history of bilateral cryptorchidism or persisting bilateral cryptorchidism compared to cases of unilateral cryptorchidism (odd-ratios were 4.9 and 2.9, respectively)[6]. In another material, about 9% (120/1405) of the testes in the series underwent a testicular biopsy simultaneously with surgery for cryptorchidism in childhood. These selected undescended testes had a 10 times higher relative risk of later development of testicular cancer than the rest of the undescended testes in the cohort that had also been operated on but not biopsied[32]. Our data, based on a large series of men operated for cryptorchidism, who all had a biopsy done at the time of the surgery in childhood, do not support the finding of a greatly increased risk of testicular cancer in biopsied testes per se. On the contrary, our data suggest a moderately increased (about two-fold) risk of testicular cancer in biopsied testes[11]. Consequently, the suggested procedure of a testicular biopsy at surgery for cryptorchidism per se is not suspected to be harmful. It may diagnose testicular neoplasia at surgery for cryptorchidism and some patients may be treated for testicular neoplasia before invasive cancer develops.

Adult men have but a very small lifetime risk of developing testicular cancer if an approximately 3 x 3 x 3 mm surgical testicular

biopsy specimen does not reveal carcinoma-in-situ-testis[33,34]. The risk in boys is different. Carcinoma-in-situ-testis was found at surgery for cryptorchidism in about 0.5% (7/1466) of boys, which is about a factor of 5 lower than the 2-3% lifetime risk of developing testicular cancer in Danish men treated for cryptorchidism[4,10,33,34]. It is very important that the patients had a risk of later development of testicular cancer even if a testicular biopsy at surgery for cryptorchidism in childhood showed no carcinoma-in-situ-testis or no germ cells at all (Table II, case 5, 6). A study similarly reported that carcinoma-in-situ-testis was not seen in three biopsy specimens from three undescended testes in two patients in whom three testicular cancers later developed. Age at biopsy was 9, 10 and 14 years and the respective ages of treatment of the cancer 20, 31 and 32 years[35]. Equivalently, carcinoma-in-situ-testis was not exhibited in one biopsy specimen from an undescended testis in a six-year-old patient who was treated for carcinoma-in-situ-testis at 17 years of age[16]. Consequently, boys are at risk of developing germ cell cancer even if a biopsy specimen at orchiopexy does not reveal carcinoma-in-situ-testis or germ cells[10,16,35]. These observations suggest that during childhood either carcinoma-in-situ-testis is not present in the testes, or it is not exhibited in testicular biopsies of all the boys in whom a malignant germ cell tumor will develop in adulthood.

Based on the literature, the excess risk for testicular cancer in cases of cryptorchidism was higher for men who were treated later than earlier in life[6,36]. In contrast, the risk of testicular cancer was not for certain elevated if surgery for cryptorchidism was done before the age of 10 years[6,37,38]. Undescended testes operated before 10 years of life, or that descended spontaneously without any treatment, were not associated with any material increase in the risk of testicular cancer. The relative risks were respectively 1.1 (95% confidence interval 0.2-8.2) and 1.2 (95% confidence interval 0.8-1.9)[6]. In a similar study, men with a history of natural descent or successful orchiopexy by the 11th birtday were not at increased risk of testicular cancer (relative risk 0.6, 95% confidence limits 0.08-5.4)[38]. In a material of 2071 cryptorchid patients who underwent surgery for cryptorchidism at median age 7.7 years (range 2-29 years), none developed testicular tumor during a follow-up at up to 30 years[37].

In general, the risk of testicular cancer in cases of cryptorchidism may depend on the existence of causal factors that affect the occurrence of both cryptorchidism and testicular cancer, on selection bias including undescended testes that have no elevated risk of testicular cancer, and on the abnormal position of the testis. Based on our data, the incidence of testicular neoplasia may be a little elevated even if surgery is done before 10 years of age, if cryptorchid patients with intra-abdominal testes, or patients with abnormal external genitalia or with known abnormal chromosomes are included. The reason is that these three categories have about a 5% risk of testicular neoplasia at time of surgery for cryptorchidism in childhood.

On the other hand, no elevated risk of testicular cancer in cases of surgery for cryptorchidism before 10 years of age may be a result of inclusion of testes that would have descended spontaneously during puberty. The incidence of cryptorchidism depends on the age of the patients. In cases of a birth weight of at least 2500 grams, about 3% of newborn boys exhibit cryptorchidism. About 2/3 of these testes descend spontaneously during the minipuberty a three months of age, and in the interval from three months to one year of age, about 1% of the boys exhibit cryptorchidism. After that age the incidence increases. Based on data obtained by interview and data obtained from the school physician's notes, about 8% of boys have cryptorchidism at some time in childhood[6,39-41]. During puberty the majority of these testes spontaneously descend, and after puberty about 1.5% of boys have cryptorchidism without treatment[41]. Testes that descend spontaneously during puberty are not associated with an increased risk of testicular cancer[6]. In the western world about 2.5% of boys undergo surgery for cryptorchidism[41]. Consequently, surgery is performed on testes which would have descended spontaneously, if the possibility had existed during the puberty of the patient[41]. With respect to the risk of later infertility this surgical procedure may be indicated, as men with bilateral spontaneously descended testes after 10 years of age had reduced sperm concentrations[42]. The increased risk of testicular cancer in cases of cryptorchidism not surgically corrected before 10 years of age may be due to the abnormal position of the testis over a longer period. The available data point to an effect of

position[6,37,38], and as a benefit of the doubt we suggest performing orchiopexy before 10 years of age to try to reduce the risk of invasive testicular neoplasia. Cryptorchidism is associated with infertility, and to reduce the risk of later infertility surgery for cryptorchidism is recommended before the patient is 1.5 years of age, especially in cases of bilateral cryptorchidism[34,43,44]. Consequently, a recommendation to perform surgery for cryptorchidism before 10 years of age to reduce the risk of later invasive testicular neoplasia may-hopefully-be very easy to follow in clinical practice. Data in the future may then help us to answer how important the abnormal position of the undescended testis is with regard to the increased risk of testicular cancer.

With respect to fertility, it is good clinical practice to make a clinical follow-up about three months after surgery for undescended testis. A history of testicular atrophy, as indicated by the response that one testis was much smaller than the other in childhood, was associated with a 2.8-fold increase (95%) confidence interval 1.8-4.2) in testicular cancer risk. The excess risk was not materially altered by stratification for cryptorchidism or inguinal hernia[2,6]. Carcinoma-in-situ-testis was reported in a 16-year-old unilateral cryptorchid boy with inguinal atrophic testis[22]. Furthermore, orchiopexy was performed before the 11th birthday in three men who developed testicular cancer, but the procedure failed in each[38].

Conclusion: In an attempt to reduce the frequency of invasive testicular cancer in cases of cryptorchidism we recommend:

1) Taking a testicular biopsy simultaneously with surgery for cryptorchidism if the testis in intra-abdominally placed, or if the patient has abnormal external genitalia or has a known abnormal karyotype, especially in cases of abnormal sex chromosomes. These clinical characteristics occur most often in patients with bilateral cryptorchidism.
2) Surgery for cryptorchidism before 10 years of age.
3) Clinical follow-up, for example three months after surgery for cryptorchidism. In cases of testicular atrophy it must be considered whether orchiectomy or a close follow-up regime for detecting carcinoma-in-situ-testis or invasive testicular neoplasia is optimal.

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