TUMEURS DU TESTICULE ET FERTILITÉ

Alain JARDIN
DESC 2005
TUMEURS DU TESTICULE

- T. GERMINALES
  - Séminome
  - Carcinome embryonnaire
  - Choriocarcinome
  - Tumeur du sac vitellin
  - Tératome

- T. NON GERMINALES
  - T. à cellules de Leydig
  - T. à cellules de Sertoli
TUMEURS DU TESTICULE ET FERTILITÉ

LE TERRAIN DU CANCER DU TESTICULE

1200 NOUVEAUX CAS PAR AN EN FRANCE

ÂGE MOYEN 27 ANS

PARENTÉ # 35 % DES HOMMES
# Risque du cancer du testicule chez les patients ayant 1 ou 2 TND

<table>
<thead>
<tr>
<th>Auteur</th>
<th>Année</th>
<th>Risque</th>
</tr>
</thead>
<tbody>
<tr>
<td>FARRER</td>
<td>1985</td>
<td>9,7</td>
</tr>
<tr>
<td>SKAKKEBAEK</td>
<td>1987</td>
<td>4,7</td>
</tr>
<tr>
<td>CAMPBELL</td>
<td>1940</td>
<td>40</td>
</tr>
<tr>
<td>HINMAN</td>
<td>1981</td>
<td>35</td>
</tr>
</tbody>
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TUMEURS DU TESTICULE ET FERTILITÉ

SPERMограмМE DES PORTEURS DE TUMEURS TESTICULAIRES

208 PATIENTS (HENDRY - BRIT. J. UROL. 1983)

54 SEMINOMES → 29% > 10M
154 NST → 22% > 10M
TUMEURS DU TESTICULE ET FERTILITÉ

CAUSES DE L' ALTERATION DU SPERMOGRAMME

AVANT TRAITEMENT

- LA TUMEUR ?
- LE TESTICULE ANORMAL ? (TND=10%)
- ANOMALIE CONTROLATERALE ? (CIS#6%)
- STRESS ?
Carcinoma in situ testis, the progenitor of testicular germ cell tumours: a clinical review.

Hoei-Hansen CE, Rajpert-De Meyts E, Daugaard G, Skakkebaek NE. Copenhagen, Denmark.

Testicular germ cell tumours (TGCT), including seminomas, embryonal carcinomas, teratomas and yolk sac tumours, have a common precursor, the carcinoma in situ (CIS) cell. Recent gene expression studies displaying close similarity of CIS cells to embryonic stem cells support the longstanding theory that CIS most likely originates in utero from fetal gonocytes. The clinical association between the testicular dysgenesis syndrome components (TGCT, cryptorchidism, genital malformations, some forms of decreased spermatogenesis) also implies a prenatal origin. Despite high cure rates of TGCT, efforts should be made to obtain diagnosis at the CIS stage, as intervention is possible before an invasive tumour develops, thus reducing the necessity for intensive therapy. CIS may be suspected in patients with an assumed extragonadal GCT or cryptorchidism, and in intersex patients and selected cases with infertility (presenting with atrophic testes and ultrasonic microlithiasis). Surgical testicular biopsy seems the only reliable diagnostic method. The management of choice of unilateral CIS is orchidectomy, or localised irradiation in bilateral cases. At least 5% of TGCT patients present with contralateral CIS; therefore, contralateral biopsy is recommended at the time of orchidectomy. Further research is warranted to identify causal factors explaining the increasing incidence of TGCT and to obtain a method of non-invasive CIS detection.
<table>
<thead>
<tr>
<th>FREQUENCE DU CIS SUR TND</th>
</tr>
</thead>
<tbody>
<tr>
<td>KRABBE 1979</td>
</tr>
<tr>
<td>PEDDERSEN 1987</td>
</tr>
<tr>
<td>SKAKKEBAEK 1989</td>
</tr>
</tbody>
</table>

CONCLUSION : BIOPSIE SYSTEMATIQUE ? NON
Question

- Fréquence du C.I.S. sur les prélèvements testiculaires faits pour I.C.S.I.?

- 5 / 766 soit 0.6%?
Testicular sperm extraction: comprehensive analysis with simultaneously performed histology in 1418 biopsies from 766 subfertile men.

Schulze W, Thom F, Knuth UA.

Abteilung für Andrologie, Universitäts-Krankenhaus Eppendorf, Hamburg, Germany.

The introduction of intracytoplasmic sperm injection (ICSI) has revolutionized treatment of male-factor infertility. Even with a single spermatozoon a pregnancy can be achieved. In cases of azoospermia due to obstruction or highly impaired spermatogenesis, spermatozoa can be retrieved directly from testicular tissue recovered by testicular biopsy followed by sperm extraction. The predictive value of histology from semi-thin sections of testicular biopsies was assessed in relation to testicular sperm extraction (TESE) results, using 1418 biopsy samples from 766 subfertile men which were evaluated simultaneously using a modified Johnsen score and an ordinal classification system for spermatozoa in TESE samples. In 655 men bilateral samples were available. Based on histological findings and TESE results, the quality of spermatogenesis in the right testes was significantly better than that in the left testes. There was a difference between the two sides in 35.7% of all patients for histology and 32.7% for TESE results. When best results from either testis were used for analysis, 76.9% of all men revealed spermatozoa in TESE preparations, although during histological evaluation of semi-thin sections only 64% of all men had shown mature spermatids. In a core group of 250 azoospermic men without anamnestic hints to obstruction and most likely to benefit from ICSI, TESE was successful in 62.8% men. Subdivision of this group dependent on follicle stimulating hormone (FSH) serum concentrations revealed that even in cases of increased FSH concentration, between 39.1 and 64.7% of men showed mature spermatids in their TESE samples. A subset of 70 azoospermic men from the main sample with symptoms and history suggestive of an obstruction and considered as positive controls showed a positive TESE result in all patients. The histology had failed to predict this in 2.9% of all cases. Nevertheless, in five men an early stage of testicular tumour (carcinoma in situ = CIS) was detected. Two of these males suffered from bilateral CIS. This reflects a prevalence of 0.7% testicular malignancy in the group of patients without a history of excurrent duct obstruction. The data demonstrate that a trial TESE with histology based on the semi-thin sectioning technique is a powerful diagnostic and therapeutic procedure, which justifies the invasive nature of sperm retrieval for ICSI. In addition, the results stress the importance of bilateral biopsies to gain optimal diagnostic and therapeutic results.
CONCLUSION

• Cancer du testicule et altération de la spermatogénèse peuvent s’inscrire dans le cadre d’une dysgénésie du testicule pouvant prendre son origine pendant la vie fœtale
• Le C.I.S. est un précurseur du cancer
  - il conduit au cancer dans 50% des cas
  - il semble n’y avoir aucune (?) évolution du C.I.S. quand le testicule qui en est atteint est irradié par une dose de 15 à 20 grays (18)
• Le C.I.S. reste très rare chez l’homme infertile!
Intratubular germ cell neoplasia of the testis: testicular intraepithelial neoplasia.

Montironi R.

Institute of Pathological Anatomy and Histopathology, School of Medicine, University of Ancona, Umberto 1 Hospital, Ospedale Regionale, I-60020 Torrette, Ancona, Italy. r.montironi@popcsi.unian.it

The observations of Skakkebaek and the evolution of the concept of intratubular germ cell neoplasia (or testicular intraepithelial neoplasia (TIN)) indicate that most, but not all, germ cell tumors of the testis evolve from a common neoplastic precursor lesion: intratubular germ cell neoplasia, unclassified type (IGCNU). It is defined as the presence of malignant germ cells within the seminiferous tubules. At 5 years about 50% of patients with a testicular biopsy positive for IGCNU have developed invasive germ cell tumors, and only a small fraction remain free of invasive tumors by 7 years. Orchiectomy is the treatment of choice in patients with unilateral IGCNU, and low-dose radiation is efficacious in patients with bilateral IGCNU (although sterility is certain). So far, there is only one published report of occurrence of two cases of germ cell cancer despite previous local radiotherapy to the testis. A recent study demonstrated an estimated risk of recurrent IGCNU following chemotherapy of 21% and 42% at 5 and 10 years, respectively.
Retentissement des traitements des cancers du testicule sur la fertilité

- Orchidectomie
- Curage ganglionnaire
- Irradiation
- Chimiothérapies
Figure 1. Semen quality after unilateral orchietomy. The percent of patients with normal sperm concentrations (>20 million sperm/mL) after unilateral orchietomy (n = 54 patients) for 4 different reasons is shown. No statistical differences are noted. (Data from Ferreira U, Netto NR, Jr, Esteves SC, et al: Comparative study of the fertility potential of men with only one testis. Scand J Urol Nephrol 25:255, 1991.)
SPERM BANKING FOR TESTIS CANCER
BICETRE EXPERIENCE
1973-1990

804 CASES

<table>
<thead>
<tr>
<th>FAILURE TO PROVIDE SAMPLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZOOSPERMIA OR SEVERE OLIGOSPERMIA</td>
</tr>
<tr>
<td>-----------------------------</td>
</tr>
<tr>
<td>SPS &lt; 0.5 x 10^6</td>
</tr>
<tr>
<td>0.5 x 10^6 &lt; SPS &lt; 2 x 10^6</td>
</tr>
<tr>
<td>SPS &gt; 2 x 10^6</td>
</tr>
<tr>
<td>5%</td>
</tr>
<tr>
<td>23%</td>
</tr>
<tr>
<td>32%</td>
</tr>
<tr>
<td>23%</td>
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<tr>
<td>17%</td>
</tr>
</tbody>
</table>

SPS: NUMBER OF SPERM PER STRAW

Université Paris Sud - Hôpital de Bicêtre
TUMEURS DU TESTICULE ET FERTILITE

ACTION DES RX SUR LA SPERMATOGENESE

EXP. SUR SUJETS SAINS (ROWLEY-1974)

0,2 GY → OATS LEGERE
0,5 GY → OATS SEVERE
0,8 GY → AZOOSPERMIE 100%
**Tumeurs du Testicule et Fertilité**

**SPERMOGRAPHISMES PRATIQUES APRES RXTHERAPIE POUR K TESTIS**

**Bicêtre : 112 Patients**

<table>
<thead>
<tr>
<th></th>
<th>&lt;1 AN</th>
<th>1 à 2 ANS</th>
<th>2 à 3 ANS</th>
<th>3 à 4 ANS</th>
<th>4 à 5 ANS</th>
<th>&gt; 5 ANS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZOO</td>
<td>74%</td>
<td>43%</td>
<td>28%</td>
<td>18%</td>
<td>12%</td>
<td>6%</td>
</tr>
<tr>
<td>&gt; 5 M/ml</td>
<td>9%</td>
<td>47%</td>
<td>64%</td>
<td>74%</td>
<td>84%</td>
<td>92%</td>
</tr>
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</table>
TUMEURS DU TESTICULE ET FERTILITÉ

SPERMOCOGRAMMES PRATIQUES APRÈS CHIMIOTHERAPIE POUR CANCER DU TESTICULE

BICETRE = 63 PATIENTS

<table>
<thead>
<tr>
<th></th>
<th>&lt; 1 AN</th>
<th>1 à 2 ANS</th>
<th>2 à 3 ANS</th>
<th>3 à 4 ANS</th>
<th>4 à 5 ANS</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZOO</td>
<td>49%</td>
<td>20%</td>
<td>6%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>&gt; 5 M/ml</td>
<td>31%</td>
<td>72%</td>
<td>90%</td>
<td>96%</td>
<td></td>
</tr>
</tbody>
</table>
TUMEURS DU TESTICULE ET FERTILITE

L’anéjaculation après curage ganglionnaire pour cancer du testicule stade 1 est passée de 60-80% à moins de 10% grâce à la préservation nerveuse sympathique lors de l’intervention.
Nerve-sparing retroperitoneal lymphadenectomy with preservation of ejaculation.

Donohue JP, Foster RS, Rowland RG, Bihrle R, Jones J, Geier G.
Department of Urology, Indiana University School of Medicine, Indianapolis.

The feasibility of sparing postganglionic fibers of lumbar sympathetic nerves during the course of retroperitoneal lymphadenectomy has been investigated at our university medical center beginning in 1978. We selected 75 patients for nerve-sparing retroperitoneal lymphadenectomy in an effort to preserve ejaculatory function postoperatively. This cohort of patients was selected on the basis of clinical stage. Of the 75 patients 73 had clinical stage I disease. However, 14 of these 73 patients had pathological stage II cancer. No patient was treated with adjuvant chemotherapy after nerve-sparing retroperitoneal lymphadenectomy. Of these 14 patients with pathological stage II disease 4 had relapse: 1 with proved retroperitoneal recurrence, and 3 with serological elevations of tumor markers and questionable clinical findings as to anatomical site of relapse. All 4 patients are free of disease after chemotherapy and/or surgical (1) rescue. There were no local recurrences in the 61 patients with negative nodes. All 75 patients ejaculate and had no evidence of disease more than 2 years after nerve-sparing retroperitoneal lymphadenectomy. It is clear that nerve-sparing retroperitoneal lymphadenectomy is a feasible technique. As noted, it can even be applied to selected patients with low volume positive nodes, yet maintaining relapse and survival figures that are acceptable. Ejaculation is reliably preserved when this nerve-sparing technique is applied accurately in retroperitoneal lymphadenectomy.
CONCLUSION

Les traitements du cancer du testicule en dehors de l’orchidectomie aggravent l’infertilité mais cette aggravation est réversible dans la grande majorité des cas.
CANCER DU TESTICULE ET FERTILITÉ

Dans de rares cas (5 à 10 %) une azoospermie définitive peut être constatée ainsi que dans 0 à 10% des curages ganglionnaires une anéjaculation.

Ces cas justifient la congélation systématique du sperme.
TUMEURS DU TESTICULE ET FERTILITE

PLACE DU CANCER DU TESTICULE DANS LA DEMANDE DE CONSERVATION DU SPERME

BICETRE : 2359 DEMANDES 1973 - 1989

<table>
<thead>
<tr>
<th>Indication</th>
<th>pourcentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>K TESTIS</td>
<td>34%</td>
</tr>
<tr>
<td>HODGKIN</td>
<td>34%</td>
</tr>
<tr>
<td>AUTRES Cancers et leucoses</td>
<td>14%</td>
</tr>
<tr>
<td>INSUFFISANCE RENALE</td>
<td>3%</td>
</tr>
<tr>
<td>AUTRES INDICATIONS</td>
<td>15%</td>
</tr>
</tbody>
</table>
Répartition des indications parmi tous les dossiers ayant donné lieu à autoconservations de 1980 à 1995

(Données sur 17 CECOS)

N = 8845

32,5%

11,8%

34,2%

8,8%

2,6%

7,9%

Pathologies auto-immunes (3)

Maladie de Hodgkin

Autres indications hémato. (1)

Cancers testiculaires

Autres cancers (2)

Nérophathies & greffes

Divers (4)

(1) - Leucémies aigues (LAL, LAM)
- Syndromes myélodysplasiques
- Syndromes lymphoplasmocytaires
  (Mycélide, Waldenström)
- LNH

(2) - Cancers digestifs
- Vesicule, Rein
- Cancers ORL

(3) - Dermatomyosite
- Myopathie
- Lupus
- Behcet
- Purpura

(4) - Malf. vésicales
- Orchi-épididymite
- Chron, RCH
- Tumours hypophysaires
- S.E.P.
- Histiocytose, Sarcoïdose
Quand et comment mettre en route une grossesse après traitement ?

• Sperme congelé?
• Naturellement après éventuelle récupération d’un spermogramme « suffisant » ?

Le moins d’assistance possible
# Use of Cryopreserved Semen at Bicêtre Hospital

## Results (Pregnancies)

Related to the quality of semen

<table>
<thead>
<tr>
<th>SPS (n x 10⁶)</th>
<th>Nb of Patients</th>
<th>Nb of Cycles</th>
<th>Nb of Pregnancies</th>
<th>IVF Nb of Cycles</th>
<th>Nb of Pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.5</td>
<td>38</td>
<td>170</td>
<td>0</td>
<td>22</td>
<td>2</td>
</tr>
<tr>
<td>0.5 &lt; n &lt; 2</td>
<td>58</td>
<td>254</td>
<td>8</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 2</td>
<td>103</td>
<td>465</td>
<td>39</td>
<td>25</td>
<td>10*</td>
</tr>
</tbody>
</table>

**SPS**: Number of sperms per straw

*1 after cryopreservation during 17 years*
TUMEURS DU TESTICULE ET FERTILITÉ

• CAS PARTICULIERS :
  Tumeurs de LEYDIG
  Tumeurs de SERTOLI
TUMEURS DE LEYDIG

• 3% des tumeurs testiculaires
• Entre 5 et 10 ans et entre 30 et 35 ans
• 95 % sont bénignes (qq malignes du vieux)
• 1/3 s’accompagnent de « signes endocriniens »
• Environ 50 % s’accompagnent d’un taux élevé d’oestradiol
• Le traitement est chirurgical et doit être conservateur
TUMEURS DU TESTICULE ET FERTILITE

• CAS PARTICULIERS :
  - Tumeurs de l’enfant
Testis-sparing surgery for benign testicular tumors in children

Foundation Lenval, Hopital pour Enfants, Nice, France

PURPOSE: In this retrospective survey we identify preoperative and intraoperative criteria of nonmalignancy and analyze the result of conservative treatment of a testicular mass. MATERIALS AND METHODS: A total of 22 surgeons responded to a questionnaire concerning lesions treated during the last 15 years in children between 0 and 15 years old. By definition alpha fetoprotein and beta human chorionic gonadotropin are within the normal limits at this age. The results were evaluated regarding evolution, growth of the preserved testis and local or distant recurrences. RESULTS: Benign tumor of the testis (83 cases) represented 48% of all cases. Orchiectomy was performed in 27 cases and conservative treatment in 56. The final histopathological diagnosis was benign germinal tumor in 48 cases, cysts in 18, gonadal stromal tumor in 13 and rare lesions (lipoma, hemangioma) in 4. No definitive clinical criteria of nonmalignancy were identified but some symptoms were suggestive of nonmalignancy. Ultrasound results were more conclusive and provided the diagnosis of teratoma, epidermoid cyst and particularly simple cyst. The conservative treatment performed 56 times was a simple biopsy in 2 children with bilateral lesions and enucleation in 52. Enucleation was performed in 43% of cases using a pedicle clamp and in 50% with frozen section. The frozen section was changed in 12 cases due to therapeutic decision for preservation (10) and orchiectomy (2). There were no contradictions between the definitive histopathological examination and frozen section. Secondary orchiectomy was performed for neonatal granular tumor. Average followup in 56 cases of conservative treatment was 4.8 years (range 6 months to 15 years). Neither secondary testicular atrophy nor any local or distant recurrence was recorded. CONCLUSIONS: A testicular tumor in children has a 50% chance of being benign. Treatment selection according to some clinical, biological, radiological and frozen section findings should allow us to decide on testis-sparing surgery without additional oncological risk, and with an aesthetic, psychological and functional benefit.
PREPUBERTAL TESTIS TUMORS: ACTUAL PREVALENCE RATE OF HISTOLOGICAL TYPES.

Pohl HG, Shukla AR, Metcalf PD, Cilento BG, Retik AB, Bagli DJ, Huff DS, Rushton HG.

From the Departments of Urology, Children's National Medical Center, Washington, D. C. (HGP, HGR), Division of Pathology (DSH), Children's Hospital of Philadelphia, Philadelphia, Pennsylvania (ARS), Hospital for Sick Children, Toronto, Ontario, Canada (PDM, DJB), and Children's Hospital, Boston, Massachusetts (BGC, ABR).

PURPOSE:: Tumor registries, urological textbooks and literature surveys all assert that yolk sac tumors are the most common primary testicular tumors in boys 12 years and younger. In contrast, several individual institutions have reported that benign tumors are more common than malignant tumors. To clarify these discordant findings, we surveyed the primary pathology records from 4 major pediatric centers. MATERIALS AND METHODS:: The pathology records of the contributing centers were culled for primary testicular masses in boys 12 years and younger. Older boys and those with either paratesticular tumors or leukemia were excluded. The prevalence of each histological subtype was calculated from the pooled cases. RESULTS:: A total of 98 patients met our criteria. Only 15% had yolk sac tumors. Teratomas comprised 48% of the tumors (mature 44%, immature 4%). Epidermoid cysts were found in another 14% of patients. Gonadal stromal cell tumors represented 13% of the total, divided among granulosa cell (5%), Leydig cell (4%), Sertoli cell (3%) and mixed gonadal stromal cell (1%). Other pathology, including cystic dysplasia (2), lymphoma (4), inflammatory pseudotumor (1) and gonadoblastoma (2), made up 9% of the total number of cases. CONCLUSIONS:: We found that benign lesions represent the majority of primary testis tumors (74%), with the most common histological type being teratoma (48%). The reported high prevalence rates of prepubertal yolk sac tumors probably results from a reporting bias, since benign tumors are less likely to be submitted to tumor registries. Therefore, the primary operative approach to the majority of testis tumors in boys 12 years and younger should entail testis sparing surgery. Orchiectomy should be reserved for histologically confirmed malignancy based on increased preoperative alpha-fetoprotein and/or frozen section analysis of the tumor.
TUMEURS DU TESTICULE ET FERTILITÉ

• CAS PARTICULIERS :

- Cancer bilatéral (d’emblée ou en 2 temps)
- Cancer sur testicule unique
- C.I.S dans le testis controlatéral

- Tumeur « incidentellement » découverte chez un homme infertile
Conservative management of small testicular tumors relative to carcinoma in situ prevalence.

Huyghe E, Soulie M, Escourrou G, Mieusset R, Plante P, Thonneau P.
, Toulouse, France.

PURPOSE: We evaluated the prevalence of carcinoma in situ (CIS) in orchiectomy specimens performed for germ cell tumors smaller than 40 mm in diameter to propose an appropriate conservative approach to bilateral tumors or tumor of a solitary testis. MATERIALS AND METHODS: Of 127 patients treated with orchiectomy between 1990 and 2002, 41 who presented with a tumor of less than 40 mm in diameter were selected for histological analysis of testicular parenchyma. The morphological items assessed were CIS, spermatogenesis and Leydig cell hyperplasia. RESULTS: CIS was observed in 39 of the 41 patients (95%). CIS was evenly distributed throughout the testicular parenchyma (ie around and beyond the tumor) in all 39 cases. Spermatogenesis was observed in 12 of 41 specimens (29%), spermatogenesis without spermatozoa was noted in 14 (34%) and absent germ cells were found in 15 (37%). Leydig cell hyperplasia was observed in 24 cases (58%). CONCLUSIONS: Histological analysis of whole orchiectomy specimens showed that CIS is almost always present in testicular parenchyma adjacent to germ cell tumor. In bilateral testis cancer or cancer occurring in a solitary testis tumorectomy plus radiotherapy appears to be the appropriate treatment in patients with a small tumor and no other risk factors. In patients who wish to father a child and have preserved spermatogenesis the natural history of CIS allows the postponement of testicular radiotherapy after orchiectomy, giving the double advantage of preserving testicular endocrine function and maintaining the possibility of natural fatherhood.
The value of the biopsy of the contralateral testis in patients with testicular germ cell cancer: the recent German experience

Dieckmann KP, Loy V.
Department of Urology, Universitätsklinikum Benjamin Franklin, Freie Universität Berlin, Germany.

PURPOSE: Testicular intraepithelial neoplasia (TIN; so-called carcinoma in situ of the testis), the precursor of testicular germ cell neoplasms can be detected by testicular biopsy many years before the clinical manifestation of the tumour. This study looked at the prevalence of contralateral TIN in patients with testicular germ cell cancer. The purpose was to evaluate this new approach of early detection of testicular cancer and to evaluate the current management strategies. Patients, methods: 1954 consecutive patients with unilateral testicular germ cell tumour underwent contralateral biopsy. All specimens were examined immunohistologically with staining for placental alkaline phosphatase. Patients with TIN were usually submitted to low-dose radiotherapy of the testis. A rebiopsy was performed after 3 months. Endocrinological evaluations were done before, during and after treatment.

RESULTS: TIN was observed in 4.9% (95% confidence intervals 3.95%-5.91%). Testicular atrophy constitutes a 4.3 fold increased risk of having contralateral TIN. 64% of the cases with TIN were found in clinically normal testes. Patients with TIN were significantly younger than those without (p < 0.017). No case with TIN was found in patients older than 50 years. Three patients developed a second testicular tumour during follow-up despite a negative biopsy. After radiotherapy, all of 23 patients had complete disappearance of TIN in the rebiopsy. After chemotherapy, 3 of 10 patients had persistent TIN histologically. After radiotherapy, 12 of 41 patients required testosterone replacement. CONCLUSION: The prevalence of contralateral TIN accords well with the known prevalence of bilateral testicular tumours. Testicular atrophy is a strong indicator for the presence of TIN but about 60% of TIN-cases occur without atrophy. Local radiotherapy to the testis with 18-20 Gy is efficacious in eradicating TIN, but it causes significant damage to almost one quarter of these patients. Chemotherapy is an unsafe treatment for TIN. This study shows the feasibility of early detection of testicular cancer in a high-risk population by means of searching for TIN. Although the management of the condition still needs refinement, the TIN-concept offers an avenue for the early detection of testicular cancer and early conservative management.
Testicular germ cell tumours (TGCT), including seminomas, embryonal carcinomas, teratomas and yolk sac tumours, have a common precursor, the carcinoma in situ (CIS) cell. Recent gene expression studies displaying close similarity of CIS cells to embryonic stem cells support the longstanding theory that CIS most likely originates in utero from fetal gonocytes. The clinical association between the testicular dysgenesis syndrome components (TGCT, cryptorchidism, genital malformations, some forms of decreased spermatogenesis) also implies a prenatal origin. Despite high cure rates of TGCT, efforts should be made to obtain diagnosis at the CIS stage, as intervention is possible before an invasive tumour develops, thus reducing the necessity for intensive therapy. CIS may be suspected in patients with an assumed extragonadal GCT or cryptorchidism, and in intersex patients and selected cases with infertility (presenting with atrophic testes and ultrasonic microlithiasis). Surgical testicular biopsy seems the only reliable diagnostic method. The management of choice of unilateral CIS is orchidectomy, or localised irradiation in bilateral cases. At least 5% of TGCT patients present with contralateral CIS; therefore, contralateral biopsy is recommended at the time of orchidectomy. Further research is warranted to identify causal factors explaining the increasing incidence of TGCT and to obtain a method of non-invasive CIS detection.
CONCLUSION

Le cancer du testicule, cancer de l’homme jeune, doit, s’il est bien pris en charge, toujours guérir et lui permettre, une fois guéri, de procréer.
Management of testicular intraepithelial neoplasia (TIN)--a review based on the principles of evidence-based medicine

Dieckmann KP, Classen J, Souchon R, Loy V.
Urologische Abteilung, Albertinen-Krankenhaus Hamburg. DieckmannKP@t-online.de

Testicular intraepithelial neoplasia (TIN; also called carcinoma in situ of the testis) is the uniform precursor of testicular germ cell tumors. There is general agreement on the biological significance of TIN, however, the treatment is still a matter of dispute. The present review summarizes the treatment options currently available. In general, the management of TIN has to be adapted to the particular clinical situation of the patient. Eradication of TIN usually implies the loss of fertility. Therefore, fertility aspects should be considered before any kind of treatment is employed. Usually, patients with TIN have only small residual potential of fertility. Nonetheless, individual patients may qualify for sperm banking or cryopreservation of testicular tissue for future sperm extraction (TESE) and assisted fertilization. The most common clinical situation is the case of contralateral TIN in the presence of unilateral testicular cancer. Low dose radiotherapy to the testis with 18 Gy is the standard management option in these patients. The same procedure may be applied to solitary testicles after partial orchietomy for germ cell tumors. During follow-up, testosterone levels should be evaluated every six months. If chemotherapy is required due to metastatic disease of the primary tumor management of TIN should be deferred. After chemotherapy 30% of TIN cases will persist and approximately 42% will recur in the later course. Repeat biopsy should be done six months after completion of chemotherapy or later. Only in cases with persistent TIN additional radiotherapy should be administered. If one testicle is afflicted with TIN while the other testis is in healthy condition (conceivable in infertility cases or patients with primary extragonadal germ cell tumors), then the TIN-bearing testis should be excised. Radiotherapy is not feasible in these cases because of shielding problems with the healthy testis.