

Sperm banking in oncofertility



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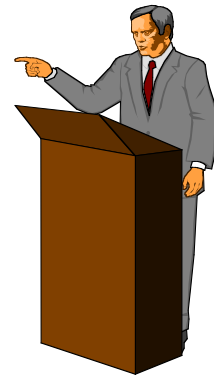


No disclosures
for information and/or research
presented in this lecture

www.inquisitor.com/wp-content/conflict.jpg

Outline

- ✓ What we all know or should know
- ✓ The controversies
- ✓ Wrap-up



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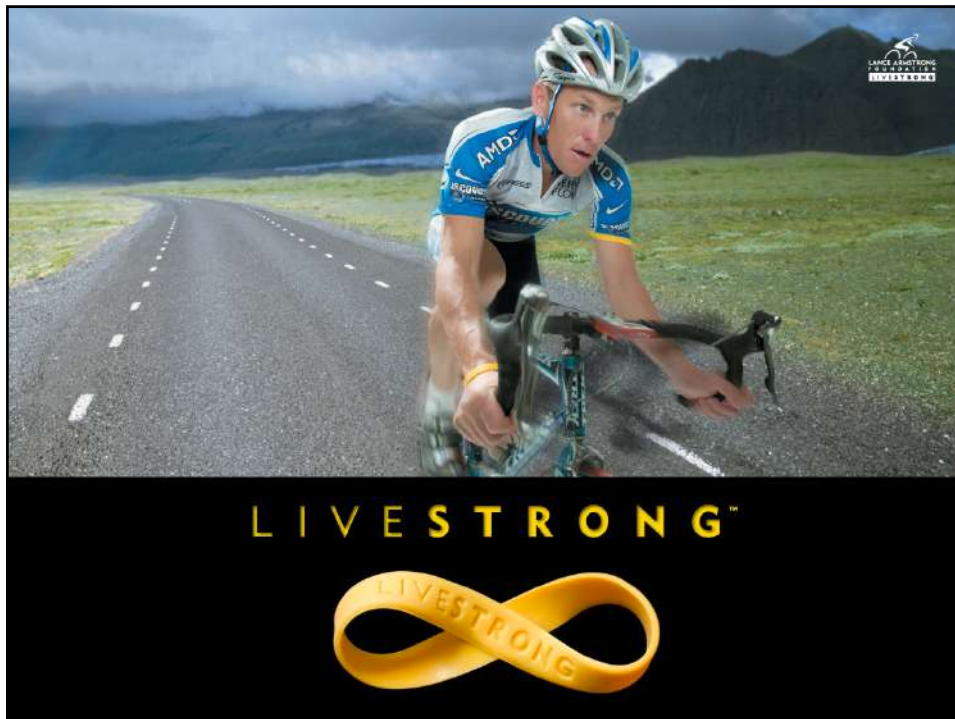


Gonadotoxicity

- proliferative spermatogenic cells are lost
- true stem cells are lost or reduced in numbers
- non-proliferative Sertoli cells are resistant
- Leydig cells are resistant
- low risk for hypogonadism
- variable risk for azoospermia/oligozoospermia

THE LANCET **Fertility preservation in men with cancer**
Herman Tournaye, Gert R Dohle, Christopher L R Barratt *Lancet* 2014; 384: 1295-301

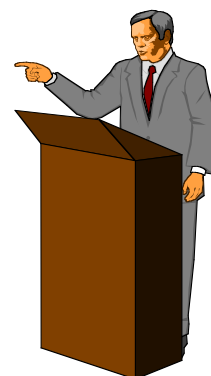
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To bank or not to bank?

Not because

- fertility-friendly protocols
- banking means postponing chemotherapy
- no banking facility nearby / too expensive
- life (survival) is more important than QOL
- not worth it

Not worth it?



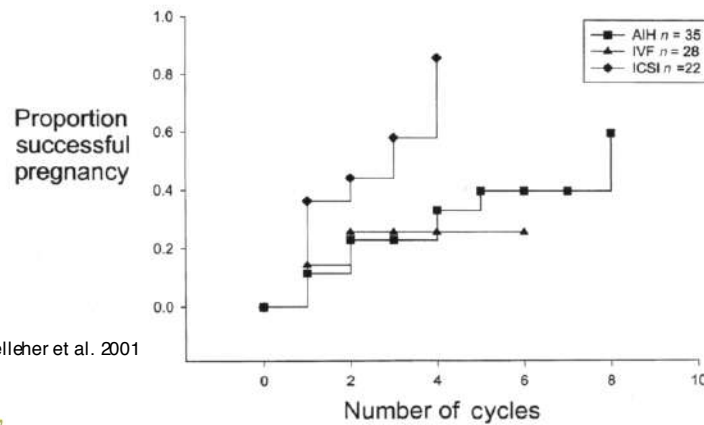
- 41 members of Irish directory
- 63% response rate
- discuss fertility problem with patients?: 73%
- facilities to bank known?: 88%
- does not delay cancer treatment?: 8% know
- ever heard of ICSI?: 54%
- unaware of role ICSI for low Q sperm: 88%

Allen et al., Ir Med J 2003

Not worth it?

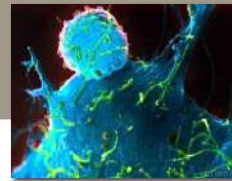


Time to pregnancy



Kelleher et al. 2001

Fertility-friendly protocols...



- Tom, 22 years old
- Hodgkin's Lymphoma Stage 4 B
- 6 cycles of ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine)
- 3 new malignant nodes: R/ MINE (methyl-glioxal, ifosfamide, vinorelbine, etoposide)
- referred for banking but (still?) azoospermic

Poor utilisation rate



- Milligan et al. 1991 (UK): 6%
- Kliesch et al. 1997 (Germ) : 8%
- Roussillon et al. 1999 (Fr): 12%
- Brussels survey 2000 (B): 17%
- Blackhall et al. 2002 (UK): 27%
- Van Casteren 2008 (NI): 7.5%



human reproduction

ORIGINAL ARTICLE *Infertility*

Survey of Reproductive Experiences and Outcomes of Cancer Survivors Who Stored Reproductive Material Before Treatment

K. Hammarberg^{1,2,*}, M. Kirkman¹, C. Stern^{3,4}, R.I. McLachlan^{5,6,7}, G. Clarke⁸, F. Agresta³, D. Gook^{3,4}, L. Rombauts^{5,7,9,10}, B. Vollenhoven^{5,9,10}, and J.R.W. FISHE¹

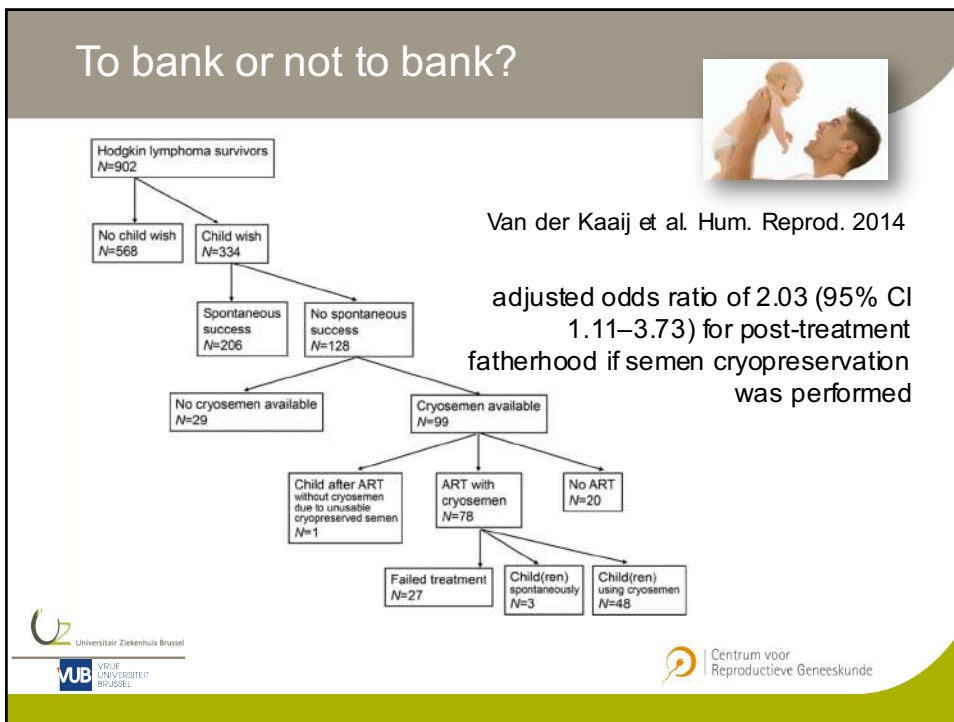
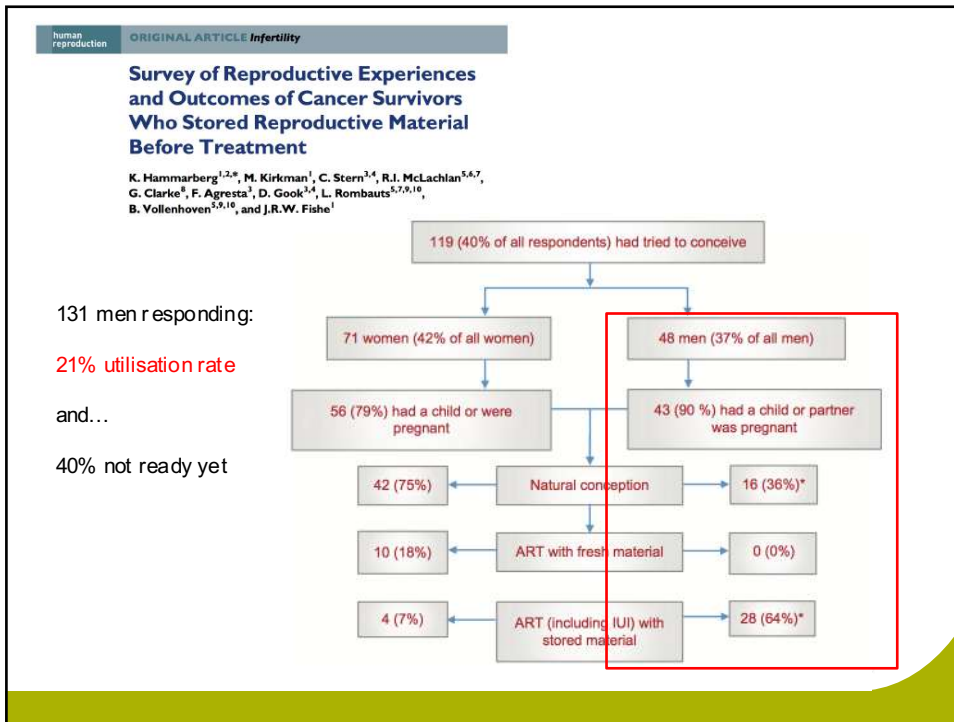
Human Reproduction, pp. 1-8, 2017

Table IV Reasons for not using stored reproductive material (n = 244).

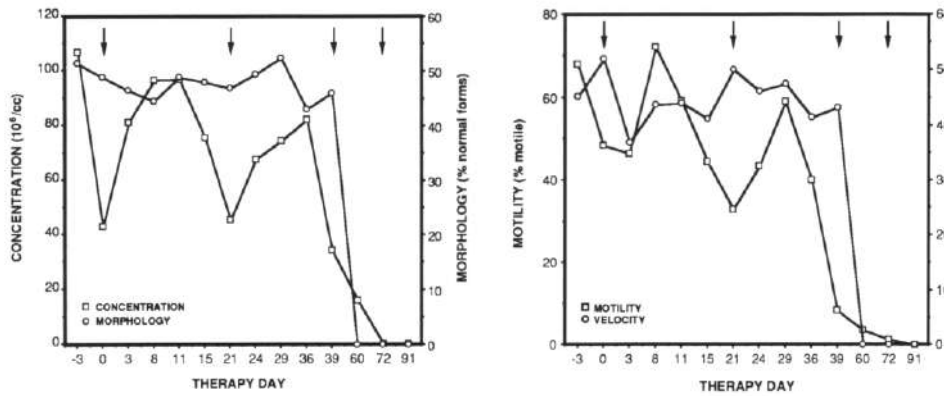
Reason ^a	All	Women	Men	P-value
I'm not yet ready to try for a baby, n (%)	102 (42)	48 (32)	54 (56)	<0.001
I plan to use it in the future, n (%)	72 (30)	41 (28)	31 (32)	NS
I/my partner conceived naturally, n (%)	52 (21)	38 (26)	14 (15)	0.04
Prefer to see whether we can conceive naturally, n (%)	48 (20)	21 (14)	27 (28)	0.007
I am not in good enough health, n (%)	18 (7)	15 (10)	3 (3)	0.04

^aMultiple reasons could be stated.





The late referral: still bank?



Carson et al. 1991 Hum. Reprod.



The late referral: still bank?

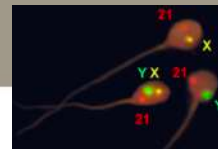


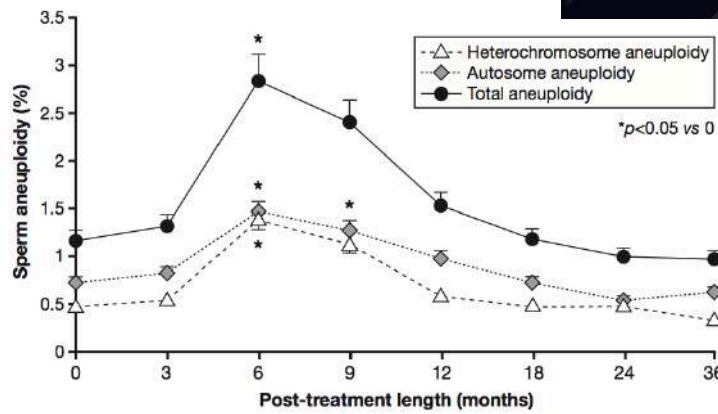
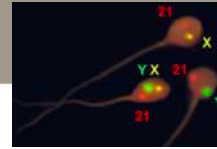
Table 1 Comparison of sperm chromosomal abnormalities pre-, during, and post-chemotherapy (CT) by FISH analysis

	Pre-CT (%)	During CT (%)	Post-CT (%)	P value
Chromosome 1				
Disomy	0.11	0.17	0.12	0.43
Chromosome 12				
Disomy	0.18	0.19	0.12	0.36
Sex chromosomes				
Disomy XX	0.05	0.06	0.10	0.37
Disomy YY	0.07	0.16	0.17	0.10
Disomy XY	0.14	0.33	0.34	0.009 ^a
Diploidy	0.10	0.14	0.29	0.005 ^b

Martin et al. 1999 Cancer Genet Cytogenet



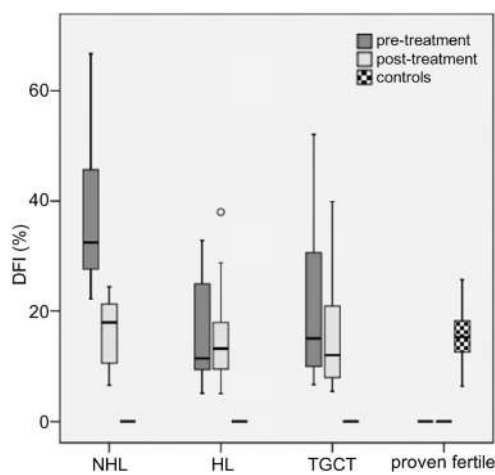
The late referral: still bank?



Burello et al. 2011 J Endocrinol Invest



DNA damage in men with cancer: a controversial issue



Smit M et al. Hum. Reprod. 2010



Risk of birth abnormalities in the offspring of men undergoing chemotherapy



Med Pediatr Oncol, 1994;22(1):33-6.

A study of children, fathered by men treated for testicular cancer, conceived before, during, and after chemotherapy.

Babosa M¹, Baki M, Bodrogi I, Gundy S.

Author information

¹ Children's Hospital Heim Pal, Budapest, Hungary.

Abstract

One hundred fifty children of 113 fathers with testicular tumour treated from 1979 on the National Institute of Oncology, Budapest, were studied. Three groups were formed on the basis of the time of conception; 69 children were born before the illness of the fathers, 40 during the 12 pretreatment months, and 41 during or after combined chemotherapy. One hundred fifty control children underwent tonsillectomy/appendectomy, but were otherwise healthy. They were matched according to age, sex, and place of inhabitation with index children. Family anamnesis, perinatal, and gestational data were listed; thereafter, physical, laboratory, immunological, and, if required, radiological examinations were made. No difference was detectable in the somatic and psychiatric status of the three groups, and development was well balanced, corresponding to age. Protocols of the combined chemotherapy applied, and the incidence of anomalies, abnormalities, malignancies, and other diseases was recorded. Incidence was similar in all three groups. Incidence of congenital malformations was not increased in children conceived before and after therapy; however, a complex congenital abnormality, an atrial septal defect with horseshoe kidney, occurred in one young girl, conceived after the end of her father's treatment. The interval between conception and the end of therapy was established in the case of children conceived either during or after therapy. This was shorter in the case of healthy children; the number of healthy children conceived during cytostatic treatment was also remarkable. Further detailed analysis of data and individual evaluation of case reports are recommended.



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The late referral: still bank?



J Natl Cancer Inst, 1991 Nov 20;83(22):1643-50.

Is there evidence of a therapy-related increase in germ cell mutation among childhood cancer survivors?

Hawkins MM¹.

Author information

Abstract

Few studies have examined human population data for evidence of an association between environmental mutagens and genetic disease. Our objective was to determine whether study of pregnancies and offspring of childhood cancer survivors would show evidence that therapy potentially mutagenic to germ cells is associated with increased risk of miscarriage, serious congenital abnormalities, or altered sex ratio. We analyzed information from patients' general practitioners for 2286 survivors of childhood cancer (1049 females and 1237 males) who were exposed or not exposed to direct irradiation of the abdomen or gonads or treatment with an alkylating agent. In addition, external control data based on the general population were used for some of the comparisons relating to congenital abnormalities and sex ratio. Data on reproductive history were complete for 1037 female survivors, who had 944 completed pregnancies, and 1078 male survivors, who produced 537 offspring. For the female survivors given abdominal or gonadal irradiation, there was an excess of miscarriages for the total number of pregnancies (17%) and for first pregnancies (19%), compared with the proportion for the total number of pregnancies in the females with similar neoplasms who were not exposed to such therapy (9%) and for first pregnancies in these females (8%). These results show re-emergence of an association suggested in our previous report of an increased risk of miscarriage as well as low birth weight among offspring of female survivors of childhood cancer who received abdominal irradiation. In that study, it was considered unlikely that the association was due to germ cell mutation. Data in the present study do not show an association of exposure to therapy potentially mutagenic to germ cells with sex ratio, or with occurrence of serious congenital abnormalities in the offspring of male or female survivors of such therapy. However, the question of a possible germ cell mutagenic effect of therapy will be adequately addressed only through an international collaborative effort.



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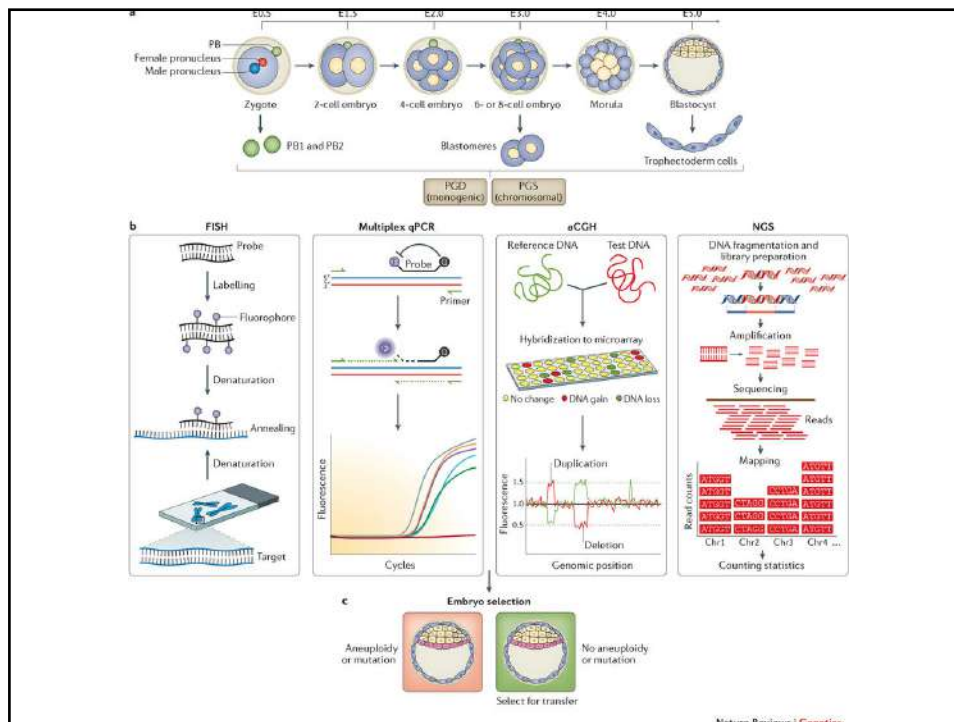
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Risk of birth abnormalities in the offspring of men with a history of cancer



- 1994 – 2005 registries Denmark and Sweden
- 1 777 765 singleton liveboms
- 8670 had a paternal history of cancer treatment
- major congenital malformations • RR 1.17 (1.05 – 1.31)
- 3.2% > 3.7%
- risk was stronger among children born within 2 years of their father’s cancer diagnosis

Stähl O, et al. *J Natl Cancer Inst* 2011;



Nothing to bank?



Azoospermia at time of diagnosis

Variable prevalence: 3 - 100 %

- Lass et al. 1998 40 out of 231 17%
- Kelleher et al. 2001 31 out of 930 3.3%



“ONCO-TESE”: TESTICULAR SPERM EXTRACTION IN AZOOSPERMIC CANCER PATIENTS BEFORE CHEMOTHERAPY—NEW GUIDELINES?

M. SCHRADER, M. MÜLLER, N. SOFIKITIS, B. STRAUB, H. KRAUSE, M. SCHOSTAK, AND K. MILLER

TABLE I. Patients with testicular germ cell tumors and azoospermia before chemotherapy

Clinical Stage	Patients with Azoospermia (n)	Patients with Successful Sperm Retrieval (n)	Patients with Maturation Arrest (JS 3-5) (n)	Patients with SCOS (JS 1-2) (n)
I	2	2/2	0/2	0/2
IIA-IIIB	8	3/8	3/8	2/8
>IIC	4	1/4	0/4	3/4

Key: JS = Johnsen score; SCOS = Sertoli cell-only syndrome.
 Histologic examination results according to clinical tumor stage; classification into clinical tumor stages followed World Health Organization guidelines.

Table II Results of testicular sperm extraction (TESE) in oncological patients with post-treatment azoospermia.

Study	Patients with TESE after chemotherapy	Positive sperm retrieval from TESE samples
Damani et al. (2002)	23	15/23 (65%)
Meseguer et al. (2003)	12	5/12 (42%)
Zorn et al. (2006)	30	13/30 (43%)
Hibi et al. (2007)	5	3/5 (60%)
Hsiao et al. (2011)	73	27/73 (37%)
Total	182	80/181 (44%)

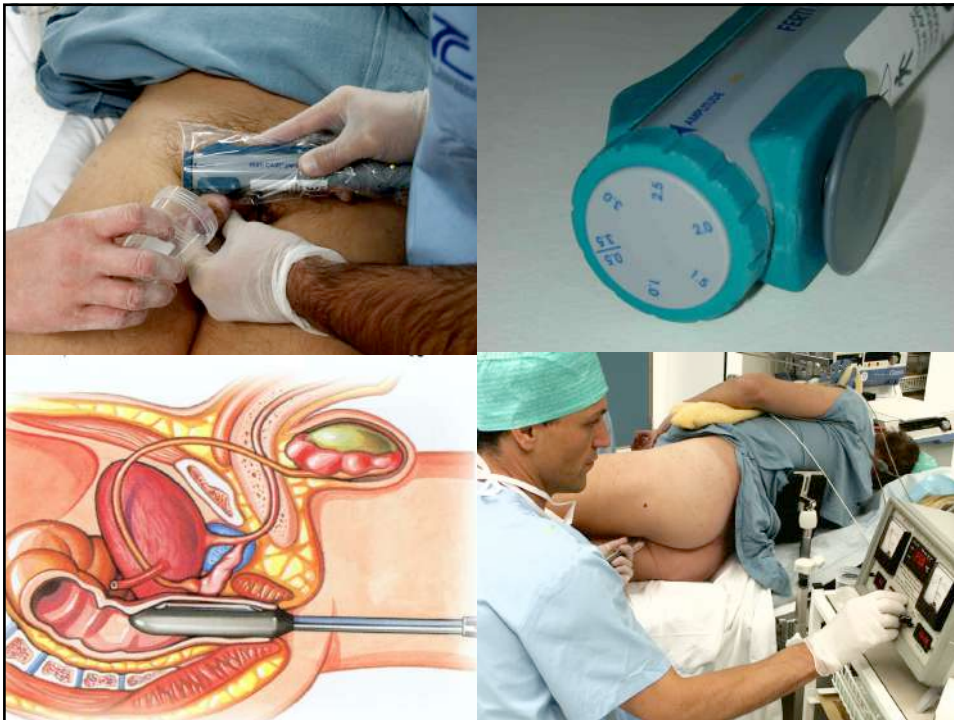
Picton et al. 2015

Too young to bank?

banking in adolescents

- after masturbation from age 14 yrs
Kliesch et al. 1996
- after penile vibrostimulation (PVS)
Muller et al. 2000
- after electroejaculation (EEJ)
Schmiegelow et al. 1998
- after TESE





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Wrap-up



- every man or adolescent facing gonadotoxicity should get his reproductive insurance
- we do have efficient preventive tools doubling the odds to become a father
- allow banking during chemotherapy?
- think beyond ejaculation

