

Impaired spermatogenesis

General recommendation
Survivors treated with one or more potentially gonadotoxic agents, and their healthcare providers, should be aware of the risk of impaired spermatogenesis and its implications for future fertility (level C evidence and supplemental literature search and expert opinion).
Who needs surveillance?
Counselling regarding the risk of impaired spermatogenesis and its implications for future fertility <i>is recommended</i> for survivors treated with: <ul style="list-style-type: none"> • Cyclophosphamide, mechlorethamine, procarbazine (level C evidence), busulfan and cyclophosphamide or fludarabine and melphalan for HSCT, ifosfamide (supplemental literature search/expert opinion). • Radiotherapy potentially exposing testes (supplemental literature search and expert opinion).
What surveillance modality should be used?
In survivors who desire assessment about possible future fertility after treatment with potentially gonadotoxic chemotherapy and/or radiotherapy potentially exposing the testes [†] , semen analysis <i>is recommended</i> as the gold standard primary surveillance modality for evaluation of spermatogenesis (expert opinion).
Clinical measurement of testicular volume and of FSH and inhibin B <i>may be reasonable</i> for identification of impaired spermatogenesis in survivors treated with potentially gonadotoxic chemotherapy and/or radiotherapy potentially exposing the testes [†] in whom semen analysis has been declined or is not possible and who desire assessment about possible future fertility. Be aware of the diagnostic limitations of these tests that may result in false positives or false negatives (level B evidence).
At what frequency and for how long should surveillance be performed?
Surveillance for impaired spermatogenesis should be performed only at the request of the survivor after informed discussion or when paternity is desired in the foreseeable future (expert opinion).
When should survivors with impaired spermatogenesis be referred?
Referral to male reproductive medicine should be offered to survivors with severely impaired spermatogenesis, defined as severe oligospermia (sperm counts $\leq 5 \times 10^6$ /ml), or those who are seeking paternity after potentially gonadotoxic chemotherapy and/or radiotherapy potentially exposing the testes, and to those whose attempts to conceive have been unsuccessful for 6 months or more, regardless of sperm count, for detailed specialist counselling or consideration of sperm cryopreservation if not already performed (expert opinion).

Testosterone deficiency

General recommendation

Survivors treated with a potentially gonadotoxic agent, and their healthcare providers, should be aware of the risk of testosterone deficiency and its implications for future health and fertility (supplemental literature search and expert opinion).

Who needs surveillance?

Counselling regarding the risk of testosterone deficiency and its implications for future health and fertility *is recommended* for survivors treated with radiotherapy potentially exposing the testes to ≥ 12 Gy or with TBI (supplemental literature search and expert opinion).

What surveillance modality should be used for pre- and peri-pubertal survivors?

At what frequency and for how long?

Monitoring of growth (height) and pubertal development and progression (Tanner stage including testicular volume)[‡] *is recommended* for pre- and peripubertal survivors treated with radiotherapy potentially exposing the testes to ≥ 12 Gy or with TBI (expert opinion).

What surveillance modality should be used for post-pubertal survivors?

At what frequency and for how long?

Measurement of testosterone concentration in an early morning blood sample at clinically appropriate intervals *is reasonable* in postpubertal survivors treated with radiotherapy potentially exposing the testes to ≥ 12 Gy or with TBI (expert opinion). In the presence of clinical signs of hypogonadism, or of previous low-normal or borderline testosterone concentrations, or if it is not possible to obtain an early morning blood sample, it *is reasonable* to measure LH concentration in addition to testosterone (expert opinion).

When should survivors with abnormalities of pubertal development be referred?

Referral to a paediatric endocrinologist *is recommended* for any survivor who has no signs of puberty by 14 years of age or failure of pubertal progression[#] (expert opinion).

When should postpubertal survivors with suspected testosterone deficiency be referred?

Referral to a specialist in male reproductive health, andrology, endocrinology or urology (according to local referral pathways) *is recommended* for postpubertal survivors treated with radiotherapy potentially exposing the testes to ≥ 12 Gy or with TBI, and in whom laboratory results suggest testosterone deficiency (expert opinion).

Physical sexual dysfunction

General recommendation

Survivors treated with one or more treatment modalities with potential to cause physical sexual dysfunction, or those who are hypogonadal, and their healthcare providers, should be aware of the risk of physical sexual dysfunction (including erectile and ejaculatory dysfunction) and its implications for future health and fertility (supplemental literature search and expert opinion).

Who needs surveillance?

Counselling regarding the risk of physical sexual dysfunction (including erectile and ejaculatory dysfunction) and its implications for future health and fertility *is recommended* for survivors:

- Treated with surgery to the spinal cord, sympathetic nerves or pelvis
- Treated with radiotherapy potentially exposing testes or pelvis
- Who are hypogonadal

(supplemental literature search and expert opinion).

What surveillance modality should be used?

Providers should take a relevant sexual history in survivors treated with surgery to the spinal cord, sympathetic nerves, or pelvis, or radiotherapy potentially exposing testes or pelvis, or those who are hypogonadal (expert opinion).

When should survivors with suspected physical sexual dysfunction be referred?

Referral to a specialist in male reproductive health, andrology, endocrinology, or urology (according to local referral pathways) *is recommended* for survivors treated with surgery to the spinal cord, sympathetic nerves, or pelvis, or radiotherapy potentially exposing testes or pelvis, or those who are hypogonadal, and who have symptoms suggesting physical sexual dysfunction (expert opinion).

Publication

Skinner R, Mulder RL, Kremer LCM, Hudson MM, Constine LS, Bardi E, Boekhout A, Borgmann-Staudt A, Brown MC, Cohn R, Dirksen U, Giwercman A, Ishiguro H, Jahnukainen K, Kenney LB, Loonen JJ, Meacham L, Neggers S, Nussey S, Petersen C, Shnorhavorian M, van den Heuvel MM, van Santen HM, Green DM. Recommendations for gonadotoxicity surveillance for male childhood, adolescent and young adult cancer survivors: A report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup Consortium. *Lancet Oncology* 2017;18:e75-e90.