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Fertility and fertility preservation

Recommendations from the society for diagnosis and therapy of haematological and oncological diseases

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- Guideline
- Conflict of interests

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1 General information

Cancer therapies (chemotherapy / radiotherapy) can lead to damage to gonadal function and loss of germ cells. However, the tumor itself can also negatively affect fertility even at the time of diagnosis, i.e. before the start of therapy. As a result, a later, biological wish to have children after the cancer has been cured may no longer be fulfilled. Impaired fertility after tumor therapy is a serious problem, especially for young adults with cancer. Due to their young age, many patients have an unfulfilled desire to have children at the time of diagnosis or have not even addressed the issue of family planning [1]. Although the cancer diagnosis raises numerous existential questions, time is also pressing to deal additionally with the topic of a desire to have children and possibilities of fertility preservation.

Even if numerous other things are running through your mind at the time of diagnosis, we recommend that you seek discussion with your treating team. Taking into account the urgency of the treatment and personal preferences, the advantages and disadvantages of fertility preservation must be weighed up and a decision made together. Psycho-oncological support can be helpful in this special and very lasting decision-making process. For an overview of information brochures or other materials, see Chapter 4 - Further links and information.

Depending on the type of cancer and the cancer therapy performed, the following side effects and symptoms may occur after treatment:

- Damage to the formation of sperm cells
- Infertility
- Menstrual irregularities
- Premature hormone deficiency (estrogen, testosterone)
- premature onset of menopause and associated menopausal symptoms.

Premature hormone deficiency (estrogen, testosterone) favors the occurrence of long-term consequences such as reduced bone density (osteopenia/osteoporosis), enlargement of the mammary gland in men (gynecomastia), increase in abdominal fat and the occurrence of cardiovascular diseases. It is often difficult to predict exactly how severely the gonads will be affected by the therapy in question and how pronounced any complaints as a result of the therapy will be. However, taking into account individual factors (see Chapter 2), it is possible to roughly estimate the risk of infertility.

2 Good to know

2.1 Why is fertility education so important for those affected?

Even though the cure of cancer is the highest priority for most young tumor patients, it has been shown that education about the risk of infertility has a great effect on psychological well-being and especially quality of life. A lack of information and thus an unfulfilled, biological desire to have children could lead to persistent psychological stress such as depression or anxiety and may permanently impair the quality of life of young tumor patients [4, 6, 8].

Keep in mind that the desire to have children of your own may change again during your lifetime. Even if you don't have a desire for children right now, it may develop in a few years.

2.2 Why is there not always education on the part of physicians?

It may be possible that your doctor has not asked you about your desire to have a child with all the information about cancer diagnosis and treatment. Often, the start of treatment is urgent and patients do not have time to think about the possible risks of infertility. For the treating team, the treatment of the cancer often has the highest priority in that case.

Many oncologists continue to complain that they sometimes do not feel experienced enough to educate patients about possible fertility preserving methods [3, 9]. Therefore, it is very important that fertility centers or reproductive medicine departments are available to which patients can be referred.

So don't be afraid to talk to your oncologist, who can refer you to appropriate contacts if necessary!

2.3 The following risk factors for the development of infertility in cancer can be mentioned:

- Type of tumor, tumor localization. It is possible that fertility is already impaired before therapy due to the tumor.
- Age of the patient at the time of therapy and thus individual fertility status/fertility reserve before therapy. With higher age, fertility may be reduced even before therapy.
- Type of therapy:
  - Irradiation (Where is irradiated? Pelvis, testicles, skull?)
  - Chemotherapy (based on the type of tumor the chemotherapy protocol is determined, different substances damage the gonads to different degrees).
- Intensity of therapy and total dose

2.4 What damage from chemotherapy should I expect?

- Women
  - the risk of permanent absence of menstruation after therapy can range from no/low risk to 20%, 40-60%, and >80% risk, depending on the chemotherapy protocol and the age of the woman.
- Men
  - in men, depending on the chemotherapy protocol, a distinction can be made between the risk of a permanent and a temporary absence of sperm production or a possible reduction in sperm counts.

Your attending physician can best assess your individual risk. Talk to him or her specifically about this so that a decision can be made in good time about the need to take further steps to preserve fertility. Ask your doctor to explain to you exactly how the fertility preservation measures work, so that you can better assess what you may have to expect.

2.5 What are the fertility preservation options for women?

- Surgical relocation of the ovaries prior to radiation therapy of the small pelvis (ovariopexy), see Onkopedia - Adolescents and Young Adults (AYA).
- Freezing of fertilized or unfertilized oocytes (cryopreservation of fertilized and unfertilized oocytes in liquid nitrogen), see Onkopedia - Adolescents and Young Adults (AYA).
- Ovarian tissue freezing (cryopreservation of ovarian tissue in liquid nitrogen); ovarian tissue is usually removed by laparoscopy, see Onkopedia - Adolescents and Young Adults (AYA).
- Drug interventions (gonadotropin-releasing hormone analogues; GnRH analogues). However, GnRH agonists are not considered sufficient as a sole option for fertility protection due to the current conflicting study situation, see Onkopedia - Adolescents and Young Adults (AYA).
- The methods can also be combined.

The decision for one of the options is based on the following criteria, among others:

- Type of tumor therapy and likelihood of developing infertility.
- Assessment of prognosis (chance for relapse-free overall survival).
- Time window until the required start of tumor therapy
- Probability of tumor-related metastasis to the ovaries
- Age at the start of therapy
- Relationship status (for the freezing of fertilized eggs, the woman must be in a stable partnership).
- Patient request
- Costs, (see also under chapter 3 Tips and tricks)

2.6 What are the fertility preservation options for men?

- Sperm freezing (obtained by masturbation before the start of therapy).
- Extraction of sperm cells from the testicular tissue (testicular sperm extraction, TESE).

2.7 Pregnancy and cancer

The diagnosis of cancer during pregnancy is an exceptional situation and requires intensive interdisciplinary cooperation between oncologists, gynecologists and psychooncologists. Depending on the underlying cancer and the resulting therapeutic pressure on the one hand, and the timing of the pregnancy on the other, the risks must be weighed and the therapy concept determined.

2.8 Desire for children in the aftercare phase following cancer therapy

In the case of a desire to have a child after a cancer therapy has been carried out, we recommend that you contact a FertiPROTEKT center. If a biological wish for a child can possibly no longer be fulfilled, adoption of a child may also be an alternative.

If pregnancy has already occurred after cancer therapy, please discuss with your gynecologist whether this results in the need for intensified care during pregnancy. This depends on both the intensity of the therapy performed and the timing of pregnancy after completion of cancer therapy. An increase in risk for adverse health effects in the offspring of former cancer patients has not been demonstrated in several studies [7]. In addition, an uncomplicated birth outcome can usually be expected [5]. Due to the increase in cardiac output during pregnancy, cardiovascular function should be monitored regularly, for example by ultrasound examination of the heart, depending on the previous cancer therapy.

3 Tips and tricks

3.1 What should I think about before starting therapy?

- The topic of fertility and possibilities of fertility preservation should be addressed promptly with the treating physicians. Close cooperation between the oncologist and the reproductive physicians is necessary here. For a desired fertility clarification, it is important to assess the risk of infertility as accurately as possible, as far as the data on the respective tumor allows. Only in this way can the decision for or against an appropriate fertility preservation measure be made in a well-considered manner.
- Prior to therapy, if the time window allows, a status of current fertility should be obtained (e.g., by blood tests/serum determination Anti-Müllerian Hormone (AMH), Follicle Stimulating Hormone (FSH), ultrasound, spermiogram).

3.2 Where can I find out about the methods and centers that offer fertility preservation?

In order to prevent possible fertility limitations and to enable young tumor patients to realize their biological wish for a child after surviving the disease, the FertiPROTEKT network has become very well established in Germany [10], see Chapter 4 - Further links and information.

On the FertiPROTEKT homepage, patients and physicians have the opportunity to obtain information about fertility preservation methods. Another concern of the network is to record in a registry all tumor patients who have received fertility counseling and/or had fertility preservation performed. Ultimately, this should also ensure standardized care at a high medical level. Referral to the FertiPROTEKT centers on the part of the oncology department is mandatory for this purpose.

In addition, several guidelines on fertility preservation in tumor patients have been developed through collaborations between reproductive medicine and oncology, such as the S2k guideline "Fertility preservation in oncological diseases" in Germany [2].

3.3 What are the costs of fertility preservation measures and who bears the costs for such measures?

The cost of sperm collection and cryopreservation (freezing in liquid nitrogen) varies depending on the center. The cost of freezing and storing sperm for 1 year is about 500 € and for oocytes about 3500-4300 €. For continued storage of tissues or cells, the annual follow-up costs are approximately 300 €. So far, not all health insurance companies cover the costs of fertility preservation measures. A change in the social law has been made in the meantime. Further links and information can be found in chapter 4, and in particular under the knowledge page on fertility of the German Foundation for Young Adults with Cancer listed there. Since January 1,

2018, young blood cancer patients can apply to the German Leukemia and Lymphoma Help for funding of fertility preserving measures, Chapter 4 - Further links and information.

3.4 How can I test my fertility after cancer therapy?

- Women
  - The return of menstruation is an important indication. It is often irregular in the first period after therapy and normalizes only slowly. A helpful laboratory value is the anti-Müllerian hormone (AMH). The value correlates with the function of the ovaries. If no pregnancy is planned, suitable contraceptive measures should be discussed with the gynecologist.
- Men
  - The recovery of sperm varies greatly from individual to individual. By means of a spermiogram, the number, shape and motility of the sperm can be assessed. Since fertilization can occur even with only a small number of sperm, men should always think about contraception (condoms) if no pregnancy is planned.

4 Further links and information

- S2k guidelines fertility preservation in oncology therapies.
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- DGHO Health Policy Series (Volume 11)
  https://www.dgho.de/publikationen/schriftenreihen/junge-erwachsene
- Onkopedia (Guidelines for adolescents and young adults)
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- FertiPROTEKT Homepage
  https://fertiprotekt.com
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  https://junge-erwachsene-mit-krebs.de/wissensbegriffe/category/fruchtbarkeit/
- German Cancer Aid: blue guidebook "Fertility and cancer
  https://www.krebshilfe.de/informieren/ueber-krebs/infothek/infomaterial-kategorie/die-blauen-ratgeber/
- German Cancer Society
  https://www.krebsgesellschaft.de/onko-internetportal/basis-informationen-krebs/leben-mit-krebs/kinderwunsch-und-krebs/kinderwunsch-und-krebs.html
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6 Gender

Gender terms used in this text represent all gender forms.

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8 Disclosure of Potential Conflicts of Interest

according to the rules of the supporting professional societies