

SKIN CANCER IN DYSTROPHIC EB (DEB)

1. Introduction

In some forms of EB, there is the possibility of developing some form of skin cancer as a serious complication. The reasons for this are still not entirely clear, but the effects are often dramatic for those affected. The earlier the signs of cancer are identified, the greater the chance is for a cure! This also applies to the dreaded skin cancer often seen with EB. Special care and attention is necessary, therefore we will make you familiar with the warning signs that you need to pay attention to in this chapter. We will also give a brief overview of the treatment options. We would like to inform you to pay attention only to the chapter that pertains to the form of EB that you or your family lives with. Only these chapters are actually relevant to you.



Important points in a nutshell

- **Risk for skin cancer**
 - **is very high in dystrophic EB**
 - **is high in junctional EB**
 - **is slightly increased in EBS generalized severe**
 - **by all others no higher than for the healthy skin population.**
- **Early detection is vital!**
- **Prevention: Regular examinations of the entire skin surface every 6 months.**
- **Warning signs: Wounds**
 - **when the healing process is too long**
 - **the wound is somehow different**
 - **is especially painful.**
- **Treatment options: all should be surgically removed.**

2. General Information Section

Cancer - this word alone makes most people shudder. Why is this by some people – yet still not with all people! Why some forms of EB develop skin cancer, has not yet been fully explained. To date very little is known about the precise cellular and molecular mechanisms that ultimately lead to tumor formation. One can imagine that in EB the repair mechanisms of the skin cells are particularly stressed during your lifetime. It now seems to be that these repair mechanisms can be restricted in their function with increasing age. Thus it may happen that sometimes skin cancer cells arise. An essential characteristic of a cancer cell is its unchecked growth. If such a cell multiplies, the body cannot prevent this. After a few weeks many skin cancer cells are already present, so that the area affected is visible. **The sooner this area is noticed, the better the chances are for a successful treatment!** It does not help to simply ignore the danger. It is much better to consciously deal with this threat, to respond quickly in the event of suspected skin cancer you can save precious time.

We need to distinguish the [different types of skin cancer in EB](#). In most cases a form called squamous type develops in the cells of the upper skin layers. This type of skin cancer is the most feared. It is a malignant tumor which starts in one location and changes into a destructive and rapidly growing tumor in the surrounding tissue and after some time also frequently metastasizes, thus forms secondary tumors.

This form of cancer most often occurs in people with severe generalized dystrophic EB. It can also occur in other dystrophic forms of EB, and occasionally with junctional EB. With increasing age the risk for skin cancer also increases, so checkups in which the entire skin is examined are more important. Unfortunately in some cases, skin cancer was found in adolescents, therefore semi-annual examinations should be the rule. Once when skin cancer has been detected, the examination must be performed more frequently, about every two or three months.

In rare cases it may also result in the formation of other types of skin cancer. A distinction must be made especially between basal cell carcinoma, which is called "white skin cancer" and a melanoma, "black skin cancer". At this point in time there is no known direct relationship with EB. There is also no indication that the incidence of these cancers is elevated in people with EB compared to people with healthy skin. The only exception is EBS generalized severe, where the risk of white skin cancer (basal cell carcinoma) seems to be slightly higher.

The possibility that you developed a form of skin cancer over the course of your life is the same for all people, so of course in people with EB. The incidence is increasing throughout the world and everyone should be familiar with the early signs of the "black skin cancer" (= melanoma) and the "white skin cancer" (= basal cell carcinoma).

Briefly summarized: When a dark pigmented mole's appearance changes, is asymmetric or has more than one shade of brown or starts to bleed, caution is advised. The same applies to reddish, rough skin areas on the head and facial area, or poorly healing areas where scabs repeatedly form. Sometimes even small nodes form on the skin that slowly grows in size. If you notice any of these early signs, you should undergo a medical examination.

The same precautionary measures that are valid for all people also apply to people with EB: Excessive sun exposure, especially sunburns should be avoided, apply a good UV protection from sunlight and perform regular mole checks.

At this point the so-called "EB nevi" should be mentioned. These are EB typical pigmentary changes that can be best compared in appearance with moles. They often occur in the area of blisters, can be quite large and are variable in shape and size. Sometimes they completely resolve and disappear. These EB nevi should always be examined during skin checks. No case has yet been described in which a pigmented nevus has developed into a malignancy, but since these pigmentary changes and the early stages of melanomas are similar, they should also be examined. So play it safe, that there no malignant skin cancer hiding among the pigment changes.

[For all forms of skin cancer: regular skin examinations cannot prevent the occurrence, but with an early recognition, therapy is often successful in many cases.](#)

DEB:

Dystrophic forms of EB unfortunately have the highest risk of occurrence for the typical EB skin cancer, squamous cell carcinoma. A significant number of patients with this form of EB develop a squamous cell carcinoma in their lifetime as a result of the underlying disease. Squamous cell carcinoma can develop over months to years and destroy and/or infest deep tissue structures during the long progression of the disease. To date very little is known about the cellular and molecular

mechanisms leading to these tumors. People with a severe generalized form are especially affected, but it can also occur in the so-called milder forms of dystrophic EB. In some cases this serious diagnosis is already made in adolescents, yet in general, the incidence of skin cancer increases with increasing age. Therefore, it is particularly important in this form of EB to be extra attentive.

It is not always easy to distinguish a dangerous skin site from other difficult wound areas. But there are warnings that you can pay attention to yourself. Many places where skin cancer has formed were first discovered by the victims themselves! You know your skin and the "normal" sequence of healing very well and if something else occurs then you notice it first.

And this is already the first and most important warning:

If a wound somehow behaves differently than another wound, you should really pay attention to it in the following days. This can mean that the healing is significantly delayed in one area. Longer delays mean that after approximately double the normal healing time of your other wounds there is no healing seen in a problem area. Or that the wound has unusually intense pain or hurts in an unusual way. The emergence of a persistent crust that is not easy to remove with ordinary methods is also such a sign. If the base of wound changes or any tissue growths occur, you should pay attention.

This does not mean that the occurrence of such a change (warning) is now skin cancer! Fortunately there are in most cases harmless causes that lead to such changes. It is often difficult to accurately detect with the naked eye whether it is a benign or a malignant change. For this reason you should consult your doctor as soon as possible so the site can be examined. He or she must then decide whether you can wait and observe the area or whether a sample is already necessary for histological examination. In case of doubt it's better to take a sample once too often than to be sorry!

How is such sampling performed?

In general, a local anesthetic is sufficient. Using a very small and fine needle, anesthetic is injected at one or more points under the skin, where the samples are to be taken. This may burn a little, but only briefly because the anesthetic works very quickly. After a few minutes small samples about 4mm-6mm in size can be clipped or cut out from the suspect area. In particularly extensive wound areas several samples often must be taken, because sometimes only a small part of such an area has malignant looking changes, and you have to make sure that you

actually find the right spots to test. After sample collection slight bleeding may occur and sometimes a suture is necessary. Usually applying a bandage is enough. Sometimes sampling is not possible under local anesthesia. For example, if the suspicious spot is too large or if it is on a particularly difficult or sensitive part of the body. Then it may be necessary to carry out the sampling under anesthesia. But since this is an additional burden on the body, we try to avoid this if possible.

The sample is then immediately sent to a laboratory in which the histological examination can be carried out under the microscope. It is very important that the person in the laboratory already has experience with the diagnosis of skin cancer in EB because it has certain characteristics under the microscope one need to know!

The analysis takes a few days and once the result is available, further plans can be made. If there is no skin cancer the wound should be treated further and perhaps a change in wound management is necessary. If cancer cells are found, the next steps should be planned rather quickly. This needs to be discussed in each case, in depth with the person concerned. Surgical removal is often possible, but in cases where large areas are involved it is necessary to plan the next steps very carefully. Sometimes minor procedures are enough and the operation may be easier, sometimes as a result of larger wounds and the location a more difficult procedure may be necessary.

In order to be honest one must also mention that sometimes you have to even think about an amputation of the arm or the leg. This is then to be considered when cancer has already developed in several places or has already spread over a larger area. Our common goal of course is to avoid whenever possible such serious interventions, so we have to take all the screenings and warning signs very seriously!

In addition to an operation other methods are now used for EB patients, such as irradiation, drug treatment for cancer (chemotherapy) or post treatment using special ointments. In both radiation therapies as well as in chemotherapy trials have so far shown little success.

For the palliative treatment and/or reduction of pain these forms of therapy can play quite a good role. In this case a close collaboration between dermatologists, surgeons, oncologists and pain specialists is necessary in every case.

It should also be mentioned that the involvement of an experienced psychologist in the planned therapy is very helpful and recommended. In order to better face the challenges of cancer therapy, patients and their relatives need any accompanying support.

Despite the screening and all surgical options the day may come when it is clear that further surgery is out of the question and all other treatment options have been exhausted. If the progression of the cancer can no longer be stopped, yet at best has slowed down, it's time to take palliative measures. This means that no longer the treatment is for the intent to cure, but with the aim to accompany the person to the end of life. This accompaniment is sufficient pain therapy and treatment of symptoms (e.g. against medication side effects, odor, etc.) as well as offering psychological and pastoral guidance. If you do have to deal with this situation, then do not try to somehow cope alone, you should look for expert help in your neighborhood. Ideally this is done with a palliative care team or a hospice team. Very often this period of care is taken over by family doctors and home health care nurses.

No one can predict how long (weeks, months, years?) this process will take therefore time is now a very precious commodity. We can all learn from the people who know that their time is limited. But in the end no man on earth knows, how much time actually remains. So use your time well, regardless of whether you are in perfect health, living with EB or affected by cancer. Think again about what is important to you in your life. Maybe it's possible to make one or the other dreams into reality. Make time for family and friends and enjoy every good day. The palliative care says that it is not so important to give life more years, but it is crucial to give more life to years!

In recent years increased research into the causes and treatment options of skin cancer in EB has taken place. Some ideas appeared promising, others are not so successful. This will hopefully change a lot in the next few years. If it should one day be necessary that you have to deal seriously with this issue, then there will perhaps be new knowledge available, which can then be safely incorporated into your treatment. But still the most important thing that will remain in the future is that cancer cells will be discovered at an early stage. The rule should be that regular skin examinations should be carried out and a biopsy should be done when there is doubt. This of course requires the courage to face this issue. Be attentive rather than closing your eyes for fear, then you will know when it is time to act and thereby gain valuable time!