DYSTROPHIC EPIDERMOLYSIS BULLOSA (DEB)

1. Introduction

Dystrophic epidermolysis bullosa is an umbrella term for all forms of EB, where the blisters are formed in the dermis layer of the skin. "Dystrophic" originates from the ancient Greek syllable "dys" and means "bad" and "trophein" for "feed" and „grow". Since the people suffering with this form are struggling with difficult food problems more than others, this gave the name to these forms. In all forms of DEB it is always the same building block or always the same protein molecule of genetic changes involved, namely the collagen 7. These changes can then lead to the collagen 7 to be completely missing, or is greatly reduced or somewhat limited in its function. There are different degrees of severity of DEB depending on the changes in collagen 7. It is important to know the exact diagnosis when DEB is suspected, if you want to adjust to the further course of the disease. In DEB in addition to the blistering of the skin there are usually additional problems that we will discuss in more detail with the different forms.

Important points in a nutshell

- **Dystrophic epidermolysis bullosa is an umbrella term for all forms of EB, where the blister formation occurs in the bottom layer of skin, the dermis.**
- **DEB is caused by different changes to a particular gene, the gene for collagen 7.**
- **The modes of transmission are different, there are recessive and dominant inherited dystrophic forms of EB.**
- **The individual forms differ significantly, depending on whether collagen 7 is completely absent, reduced and/or limited in its function.**
- **In addition to the blistering on the skin, there are often additional problems (involvement of the mucous membranes, changes to the hands, among other things).**

2. RECESSIVE DYSTROPHIC EPIDERMOLYSIS BULLOSA (RDEB)

All forms of recessive dystrophic EB are caused by mutations in the gene for collagen 7 as the name implies, these forms are inherited as autosomal recessive. For more detailed explanations, see the chapter „Genetic".

Depending on how pronounced the changes to the collagen 7 building block affect the skin is how we distinguish the following forms:

- **RDEB difficult to generalise (formerly called DEB Hallopeau-Siemens)**
- **RDEB generalized other**
- **RDEB inversa**
- **RDEB pretibial**
- **RDEB pruriginosa**
- **RDEB centripetalis**
- **RDEB-BDN**

With each RDEB-form there are very large differences in the course they take. When confronted with a diagnosis of RDEB, you should first ask if it is definitely clear which form of RDEB you have, because the further course of treatment depends on which form you have. Unfortunately the exact EB-type can often not be determined from the outset, even if the genetic findings are already present.

As long as there is an uncertainty as to which form of RDEB you are dealing with, you should read our additional information with caution. It may be that you give yourself unnecessary worry on the one hand and on the other hand, it may also be that you have high hopes that are ruined. It is especially important in this situation that you quickly find an experienced medical partner who helps you to correctly classify this information for your situation!

If it is a milder variant of RDEB, it is possible that some of the problems described below may actually occur. It may be that you are still faced with the fact that you may have some problems yet with less severity and it hardly affects your life. There are many levels of severity possible for each of the individual RDEB forms.

It is different with severe generalized RDEB. When it is certain that you are dealing with a particularly severe form of recessive dystrophic EB, you must be prepared that with this diagnosis your life will change completely. Especially if you are a

parent of a child affected with this disorder. It's hard to find proper words to make you comfortable with this situation, but it should at least be tried. However, we point out that it is essential that you discuss everything you read here with a specialist for EB and/or a doctor you trust.

We will now describe successively the problems associated with RDEB. We will try to point out how pronounced each of the problems can be in the different forms. This is not an easy task, because everyone may experience these problems differently. In our clinic we are regularly confronted with completely different combinations of these problems. You most often hear the phrase: "It seems as if everyone has their own form of EB." Still, it makes sense to us, to at least give an overview of the possible effects of RDEB. Only when you know what to look for, you can learn to deal with it and/or make provisions.

The first weeks of life may proceed differently for each individual. In some children only a few blisters emerge while in others severe blistering can appear very threatening. A baby with a RDEB must therefore be well observed, in order to respond in time for infections or other problems.

In RDEB blistering normally begins at birth. In the generalized form blisters can occur on the whole body, in the other forms they occur only on individual parts of the body. In the generalized forms very large areas of the body can be affected, which may make the care of the wounds a time-consuming and difficult process. Inflamed and purulent wounds may also complicate this situation. When the blisters heal, scars remain for all RDEB-forms; also a slight atrophy of the skin is partially created in areas of heavier blistering. With the severe form affected children and adults also often suffer from severe pain and agonizing itching, therefore a concomitant drug therapy may be necessary.

A common but harmless side effect with RDEB is the formation of milia in regions where blisters heal. Milia (derived from the Latin word for "millet") also called "Semolina" are very small white cysts that can form on the skin at the opening of sebaceous glands. Although they are in themselves harmless, they are often perceived as disturbing by those affected.

Some sufferers are also observed to have skin discoloration, which are probably caused by pigmentation in areas where blisters arise. These pigmentary changes are harmless in themselves, but are often felt as disturbing by those affected as the

skin appears blemished. Regular inspections, especially of areas with darker pigmentation, are necessary to make sure that no malignant change (= skin cancer or precursors of skin cancer) are hidden.

If you do research on information about the recessive forms of EB, you will surely be confronted with images of severely crooked finger; also there are often images of hands where the fingers are completely grown together. It is a fact that these distortions, or "contractions", and the growing together of the finger in the severe generalized RDEB-forms are very common. You cannot predict how quickly these changes occur, for individual cases.
Unfortunately in the severe generalized RDEB these changes of the hand often develop at an early age. Over time it can lead to total inoperability of the hands, when no delaying or preventive measures are taken. With other generalized forms these changes usually occur later, develop slower and are not so pronounced. With all the other forms they very rarely occur.

These same changes also affect the toes and feet. Treatments in this area are difficult, but not always necessary. The functionality of the feet is often not severely restricted, walking and holding your balance should be possible as a rule. However exceptions are possible, especially if severe blistering and painful sores on the soles of the feet occur. Physical therapy should be a part of therapy from the beginning, as it helps to avoid problems with walking from developing.

In all forms of RDEB there may be changes and/or loss of the nails, on the fingers and toes. Preventive measures have been tried, yet so far without success.

In RDEB the mucosa of the mouth, esophagus and gastrointestinal system is regularly affected. Blisters and sores in these areas can lead to consequences such as difficulty swallowing, narrowing and stiffening of the esophagus. Thus, the intake of food is difficult.

How severe the problems are is different in each case. Experience has shown that most people with a severe generalized EB and RDEB inversa are particularly affected, but also in other forms of RDEB eating can be a problem to provide good nutrition. Therefore, from the start a good dietary consult is advised to ensure adequate nutrition and to avoid subsequent problems. Consequences of poor nutrition such as anemia, vitamin deficiency, and lack of protein, growth retardation or a delayed onset of puberty can be avoided. Additional high-calorie food and the

addition of vitamins and trace elements are always necessary and really helpful in severe cases of EB. For more information, see our chapter „Nutrition".

The stress that your body is exposed to by constant formation of large wounds and a difficult nutritional state for a long period of time, can also cause problems with internal organs such as the heart and kidneys. These organs must be examined regularly, so you can make timely treatment when there are decreases in their function.

The involvement of the oral mucosa is observed in most cases of RDEB. The resulting complicated oral hygiene promotes the development of caries. Therefore, in RDEB the teeth and oral hygiene should be given special attention. When the first tooth appears dental checks and professional teeth cleaning should be performed regularly.

In all forms of RDEB sticking together of the eyelids and blistering of the cornea can often reoccur. Very painful closure of both eyes often lasting several days is the result. In severe forms it is seen more often, but occasionally it can also affect people with mild RDEB. For more information, see our chapter „Eyes".

During the hot weather in summer almost all those people affected complain of increased blistering. Heat and also sweating promote the formation of blisters, so it is as a consequence more common than usual at this time to form open sores and scabs.

The prognosis and life expectancy is quite different between the RDEB - forms, ranging from very mild to very severe progression, which are overshadowed by many additional problems. Individual cases cannot be predicted, from the beginning one has to observe the progression of the disease closely. Good medical monitoring is necessary during your whole life in every case.

In life expectancy, several factors play a major role. The two outstanding problems are the possible development of skin cancer and the difficult nutritional situation, from which the resulting problems can be life threatening. Early detection of skin changes are important, so already discovered precursors of skin cancer can be quickly removed preferably by surgery. This is especially true for the generalized forms of RDEB, but can in rare cases also affect all other forms REDB. Therefore

regular checkups must be carried out no later than puberty, with skin checks in addition to the necessary treatments.

Now a few comments on the individual subtypes of RDEB, each being characterized by:

RDEB generalized severe:

This is the most severe form of RDEB. All of the above described problems can occur and be a burden in different ways. But of course cannot be predicted in individual cases, besides the particularly severe cases, milder variants are known.

RDEB generalized other:

Even though blister formation over the whole body is possible, the severity and additional problems that can occur are however generally much milder in comparison to the severe generalized form.

RDEB inversa:

„Inversa " means „inward". In this form the skin is only slightly problematic, but the mucous membrane of the mouth, esophagus and gastrointestinal tract are severely affected in comparison. Blisters and sores in these areas lead to difficulty swallowing, and narrowing and stiffening of the esophagus.

Pretibial RDEB:

In this form the blisters, still for unknown reasons, are mainly restricted to the area of the front of the lower leg („pretibial"= „in front of the shin"), but also blisters occur relatively frequently on the hands and feet.
Nail changes and loss are common. Additional problems are rare and in general a rather mild course can be expected.

RDEB pruriginosa:

„Pruriginosa„ means „itchy ", indicating that the main feature of RDEB pruriginosa is that the itching is particularly severe. The blistering is often not so pronounced; or it may be generalized or limited to specific parts of the body. Other problems are rare, but cannot be excluded.

RDEB centripetalis:

The blistering is usually limited in this form to the shin area, also nail changes and loss are often observed. Rarely, yet also involvement of the mucous membrane in the mouth can occur.

RDEB – BDN:

„BDN" means "dermolysis bullous of the newborn“, which can be roughly translated as "blistering peeling skin of the newborn”. In this special form, large blisters develop after birth, but then the blisters heal relatively quickly. In the further course of the disease no more blisters are observed .This may initially look quite dramatic, yet the babies should just be well observed and treated like all other newborns with EB.

One must be aware that there are also other diseases of the newborn, which initially look similar, but they require completely different treatment. There should be no confusion. In RDEB-BDN there are no more blisters formed after a few weeks, or only very rarely. So this is a temporary condition. This form of EB is very rare and you should always wait until the diagnosis is in fact established.