Epidermolysis **B**ullosa

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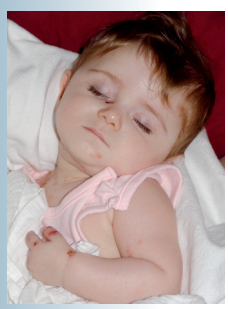
Clinical Picture

Epidermolysis bullosa (EB) is a rare inherited genetic condition in which the skin and internal body linings blister as a result of even slight rubbing or bumping, causing painful blisters and open wounds. In individuals without EB, the two layers of skin (the epidermis, the outer layer, and the dermis, the inner layer) are held together so that they do not move independently. In individuals with EB, the two layers can move independently and any friction between them creates the blisters or sores that are often compared to third-degree burns. The overall prevalence of EB is estimated at one per 10 000 persons and affects both males and females equally. There are three forms of inherited EB, EB simplex, junctional EB and dystrophic EB. These different subtypes are defined by the depth of blister within the skin layers.



Sakura, epidermolysis bullosa
© Stefaan Van Rossem.

There are also acquired forms of EB that have very similar symptoms to the inherited forms. The onset of inherited EB usually occurs at birth or shortly after, whereas acquired EB usually appears later in adulthood. Patients with EB simplex sometimes have blistering that is confined to the feet and hands and often do not require significant medical assistance. In another form of EB simplex, however, blistering can occur all over the body and requires more medical attention. Approximately half of the patients with junctional EB do not survive past their third year of life, due to malnutrition and anaemia caused by serious blistering in the pharynx and the oesophagus. Other individuals suffering from junctional EB do not experience any life restrictions. There is a wide variation in the severity of dystrophic EB. In general, dystrophic EB is not life-threatening in childhood. At its least severe (this is often the dominant inheritable type of dystrophic EB) the patient can lead an almost normal life. However, the severity of the disorder does increase at a later age due to scarring, fusion of fingers and wasting of skin tissue. In the recessive type of dystrophic EB, there is a high chance of developing a squamous cell carcinoma (a potentially lethal skin cancer) before the age of 35 years. Although there is no cure for EB, many complications can be avoided or minimised through prevention of infection, protection of the skin against trauma, attention to nutritional deficiencies and dietary complications, and minimisation of deformities.

'From what I know of children with EB, they seem to be blessed with big personalities that shine out and say more about them than any medical condition ever could.'
Marie, mother of two daughters with EB

Living With Epidermolysis Bullosa

Patients with EB are some of the most fragile of all rare disease patients. However with the help of healthcare professionals, careful daily hygiene and a positive outlook, patients with EB can enjoy a good quality of life. The symptoms experienced by people with EB vary, but blistering and pain are common symptoms to all types of the disease. For patients in which blistering also affects the inner body linings, such as the mouth and the oesophagus, eating solids is almost impossible, and the disposal of the body waste extremely painful. When this condition applies, malnutrition is often a consequence, further reducing the body's resistance to infection.
For infants, dressing and undressing, bathing and changing are delicate tasks sometimes heartbreaking to perform. In its most severe form, EB is fatal in infancy. Younger children, who like to move around and play, must keep their skin dressed when others do not have to, such as in warm weather and around swimming pools. In severe cases of EB, scarring after blister formation may cause fusion of the fingers and toes. Both of these aspects of life with EB can provoke unwanted attention and questions from strangers.

'As a young woman, I like to dress up for an evening out, maybe wearing a nice dress with pretty shoes. But as a woman with EB Simplex, it is not that easy. Dresses do not look so good worn with trainers, and sandals do not look so good worn with blisters.'
Elizabeth, 26

Children with EB are encouraged to attend normal schools. However a school day for a student with EB may be much more of a challenge than for other students. Children with EB must begin their day much earlier than other students as frequent bathing, the application of creams and oils, and reapplication of bandages under soft clothes and shoes take extra time. If walking is too painful, mobility aids such as an electric scooter are helpful. Teachers must be aware of their fragile state and make sure that children are careful not to engage in activities that can harm them.
Adults with EB also experience limitations. Some people with EB are perceived as lazy when they cannot walk far or keep up with the physical demands of adult life. They are limited in the work that they can do as they cannot stay on their feet for long periods of time. Leisure activities that require physical exertion such as sports and travelling are also not always possible due to physical limitations presented by the disease. Women with EB may decide to have children only after careful evaluation of the associated risks. Frequent visits to the hospital are needed by all patients to check skin, iron levels and nutrition. Patients with EB may be at increased risk of squamous cell cancer of the skin and should be regularly monitored.

Access to Medical and **Social Services**

PARTICIPANTS IN THE SURVEY

Responses from 249 families of EB patients from ten countries were analysed in the survey *(Figure 1)*. More females (56%) responded than males (44%). The mean age of patients was 26 years (age at diagnosis: 5 years).

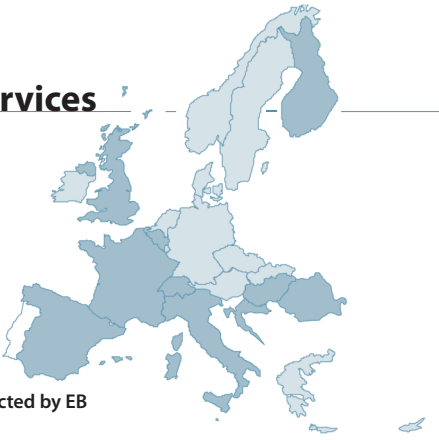


Figure 1 Survey participants affected by EB

NEED FOR MEDICAL SERVICES

Overall, patients with EB needed eight different kinds of medical services related to their disease (slightly less than the average nine medical services for the 16 rare diseases surveyed).

Not surprisingly, dermatology was the most frequently sought consultation (80%), followed by ophthalmology (34%), paediatrics (24%) and emergency services (23%) *(Figure 2)*. Respondents sought the remaining 12 types of consultations (nutrition, gastroenterology, internal medicine, haematology, orthopaedics, ear-nose-throat medicine, genetics, pain control, gynaecology, oral and maxillofacial medicine, cardiology and foot medicine) 13% to 19% of the time. The most frequently needed explorations were biological testing (59%), microbiology (32%), biopsy/cytology (31%), radiology (26%), ultrasound (23%), ECG (17%), genetic testing (13%) and specialised imagery (13%). Other types of care sought included nursing care (44%), dental care (43%), surgery (29%), glasses (26%), physiotherapy (26%), psychotherapy (25%) and injection (20%). Hospitalisation occurred in 55% of patients for an average total duration of 19 days.

'I have a one-to-one helper to help set up my computer equipment for my art and design course, and once it's set up, I can work on it independently. The students in my class have accepted my condition and they get on fine with me. I get around college on my scooter, and if the lessons are upstairs and my feet hurt, I use a lift as well as a manual wheelchair to get up and down the floors with the help of my caretaker.'
Dean, United Kingdom

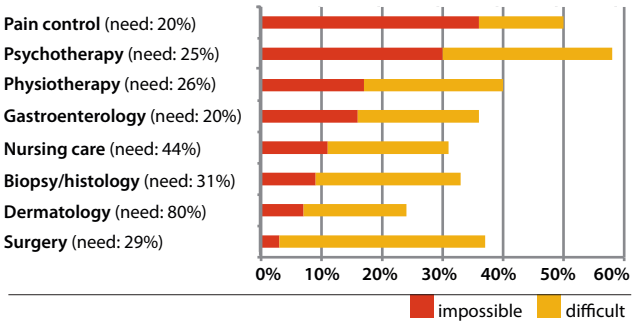


Figure 2
Need for and access ` to eight representative medical services for EB.

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 13% of situations overall for EB patients

Pain control services were impossible to access for 35% of patients. Access was impossible for 30% of respondents to psychotherapy, 17% for physiotherapy and 15% for gastroenterology consultations.

In contrast, very few EB patients (3%) found it impossible to access surgical services. A lack of referral was the most frequent barrier to access: 100% for surgery, 75% for gastroenterology, 67% for psychotherapy, 57% for biopsy/histology and 56% pain control services. Unavailability of the service was also a significant barrier to access for pain control (56%), nursing care (42%) and dermatology (38%) services. Personal cost was the most significant barrier for psychotherapy (22%). Waiting time for obtaining an appointment was considered a hurdle in accessing dermatology

(31%), pain control (28%), physiotherapy (27%) and psychotherapy (22%) consultations. Excessive distance from the medical structure was reported as a barrier to access for dermatology (38%), psychotherapy (28%) and gastroenterology (25%) services. Difficulty in travel prevented patients from accessing gastroenterology (25%), nursing care (25%) and dermatology (23%) services.

Access to medical services was difficult in 22% of situations

Respondents experienced difficult access to surgery (34%), psychotherapy (28%), biopsy/cytology (24%) and physiotherapy (23%) consultations. The number of appointments was considered insufficient for psychotherapy (34%) and physiotherapy (21%) services. Personal cost was considered excessive for nursing care (50%), physiotherapy (50%), surgery (47%) and psychotherapy (40%). Access to the assistance of a professional for the journey to a medical structure was not frequent, overall 8%.

Satisfaction with medical services

Overall, 85% of patients felt that medical services responded fully or partially to their expectations, with low variability between medical services *(Figure 3)*.

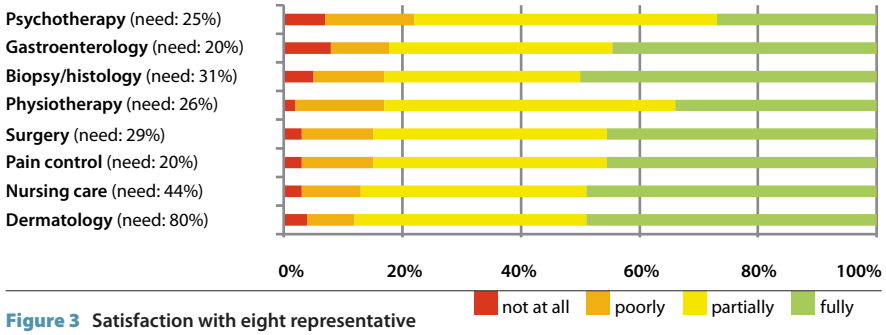


Figure 3 Satisfaction with eight representative medical services for respondents affected by EB

SOCIAL ASSISTANCE

Amongst the 32% of families needing social assistance, 4% failed to meet with a social worker and 25% met one with difficulty. The level of satisfaction overall was 55%, with low variability in relation to the kind of assistance *(Figure 4)*.

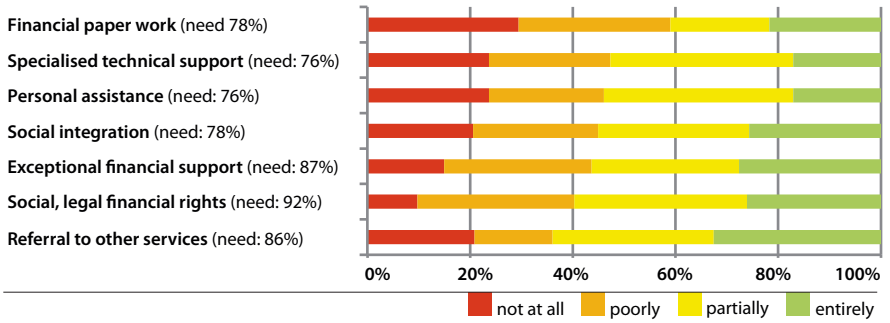


Figure 4 Satisfaction with specific social services for respondents affected by EB

REJECTION

Patients with EB experienced rejection by health professionals more frequently (28%) than respondents for the other 16 surveyed rare diseases (overall 18%). The reluctance of the health professional due to the complexity of the disease was the main cause of rejection (96% of cases). Rejection due to a physical aspect was less reported (8%). Disease-related behaviour (2%) and difficulties in communication (5%) were rarely considered as causes of rejection. The frequency and cause of rejection varied according to the patient's country of origin *(Figure 5)*.

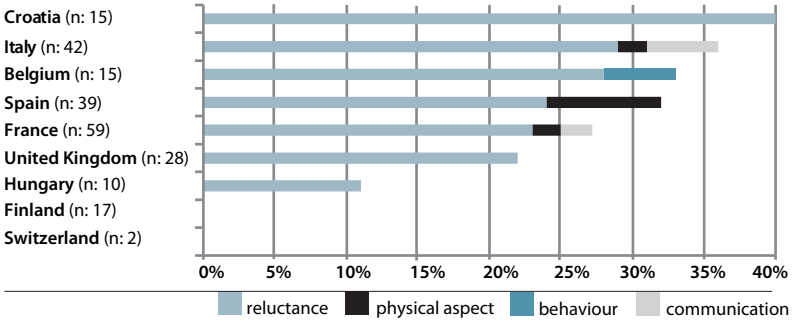


Figure 5 **Cumulated frequencies of causes of rejection by country (n: total number of respondents) in EB. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.**

CONSEQUENCES OF THE DISEASE

In 56% of families, one member had to work less or stop his or her professional activity. In 20% of cases the patient decreased his or her professional activity and 36% of respondents decreased their professional activity to take care of a relative. As a consequence of the disease, 14% of patients had to move house. The majority of these patients had to move to a more adapted house (47%) or to move closer to a relative (35%), however patients also moved to be closer to disease specialists (24%) or to an adapted care centre (9%).

Expectations Regarding **Centres of Expertise** for Rare Diseases

Not differing from the overall opinion of survey participants, respondents with EB considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels

- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

Survey participants with EB also ranked the 'informing patients about their rights and guiding them toward social services, schools, leisure activities, or vocational guidance, etc.' as the fourth most essential function provided by a Centre of Expertise. As EB patients reported particularly difficult access to social services, it is not surprising that this function of a Centre of Expertise was considered important.

Reaction to Results

In addition to those investigated in the survey, two additional services should be emphasised as important for EB patients: dental care and pain management. The lack of referral to needed services often results from the fact that general practitioners may have very little knowledge about EB and not recognise the need for specialised care. In some isolated cases, specialists have preferred to 'keep' EB patients as a result of a personal interest in investigating the disease, often at the expense of the patient's well-being.

Lack of access to essential services is not usually due to the unavailability of the services, but rather to difficulties such as the need to be accompanied or a long waiting time to obtain an appointment. The lack of satisfaction with medical services may result from the absence of one crucial professional in a multidisciplinary team. Information about the best EB treatment is often provided by patient organisations.

The rejection experienced by EB patients may be linked to the cultural and moral stigma associated with severe dermatological diseases. The pathology of the diseases means that patients have many limitations and difficulties. For example, the scarring of the hands means that in school some students might need assistance or an alternative means of writing. Unfortunately the scarcity and inadequacy of social services makes it difficult to access this type of assistance.