Epidermolysis bullosa (EB)

NHS Learning Hub Module

August 2025

GET STARTED

debra
THE BUTTERFLY SKIN CHARITY

Cuttsy &Cuttsy®

Why is this learning important?

Epidermolysis bullosa (EB), is a rare, heterogenous group of inherited skin disorders that causes extreme skin fragility, leading to painful blistering with minimal mechanical friction or trauma.

EB can affect not only the skin but also mucous membranes, the epithelial-lined tissue and internal organs, significantly impacting quality of life.

There are **currently no curative treatments** for any of the four major classic types of EB or their subtypes. Accurate diagnosis and timely referral are crucial for effective symptom management and long-term care.

EB shares clinical features with a range of other conditions — from immunobullous disorders to more common infections such as impetigo or tinea — making **differentiation in primary care both essential and challenging**.

*EB is also known as **mechanobullous disease** and commonly referred to as '**butterfly skin**'.*

You have an important role

Primary care professionals play a key role in recognising the signs of EB, initiating appropriate investigations, and ensuring patients are referred to one of the UK's specialist EB centres.

By completing this training, you're helping to promote earlier recognition, faster access to specialist care, and better outcomes for people living with EB across the UK.

LIVING WITH EB

Living with EB

The following photos highlight some of the cutaneous manifestations of EB, allowing us to have a brief insight into what living with EB must be like for patients.

What will you learn?

This interactive training has been designed to raise awareness about EB for healthcare professionals.

By completing this module, you will be able to:

1. **Recognise key clinical features** of EB during patient consultations
2. **Differentiate EB** from at least three common differential diagnoses and outline appropriate first-line investigations
3. **Summarise** the **UK epidemiological** data and inheritance patterns for the four main EB subtypes
4. **Classify** and **describe the four major subtypes** of EB (EBS, JEB, DEB, KEB) with typical clinical presentations
5. **Demonstrate appropriate referral pathways** for suspected EB cases within the NHS
6. **Explain** the **diagnostic confirmation process** and outline current **management strategies** for EB

DEB, dystrophic epidermolysis bullosa; EB, epidermolysis bullosa; EBS, epidermolysis bullosa simplex; JEB, junctional epidermolysis bullosa; KEB, kindler epidermolysis bullosa.

How to use this module

Training should take approximately **1 hour**, but take your time and work through it at your own pace

Use the '**next**' and '**previous**' arrows to navigate through the module

Your quiz scores **will not be saved** and are simply to assess your own learning

Before we begin...

Please complete this pre-learning quiz to see what you already know about EB.

We'll revisit the same quiz at the end of the module to see how your understanding has improved, so don't worry if you don't know too much at this point.

START THE QUIZ

CONTINUE WITH TRAINING

The quiz is not timed.

Let’s meet Harry

Harry is a 13-year-old boy who presents with his mum in a routine appointment.

We will follow Harry’s story as we progress through this module.

1. **Clinical presentation and differential diagnosis of EB**
   Blistered feet and pain while playing football
2. **Epidemiology of EB**
   Establishing the family history with mum, Samantha
3. **Classification of EB**
   Determining the type of EB Harry has
4. **Referral to an EB centre**
   Harry and his mum are referred for accurate further care
5. **Confirming the diagnosis and management**
   Both receive precise diagnoses with expert support and management of symptoms

Let’s see how Harry presents to you in your clinic.

1. **Clinical presentation and differential diagnosis of EB**
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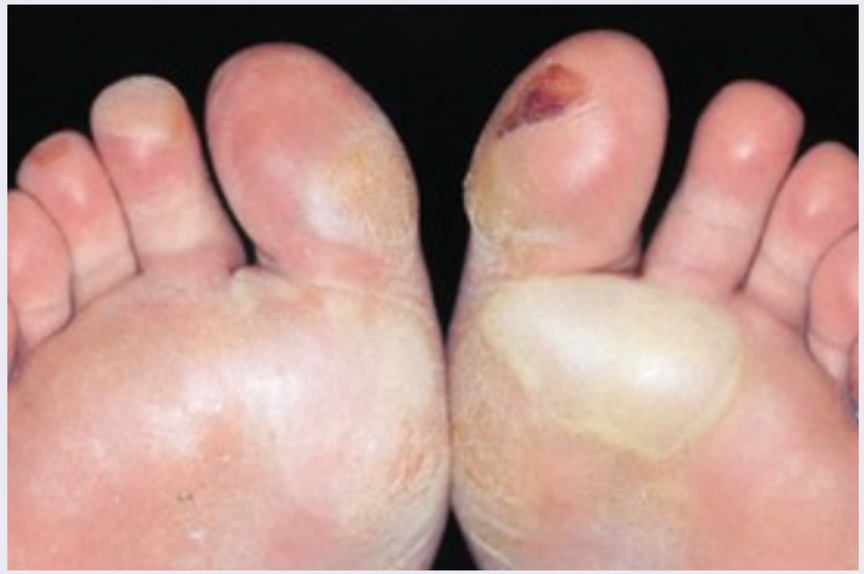
Clinical presentation and differential diagnosis of EB

Harry and his mum Samantha, want to discuss the **painful blisters on Harry's feet**, which are affecting his ability to play football.

Harry has always noticed his skin is more susceptible to blisters compared with his friends.



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QUESTION 1

Which of the following could be potential differential diagnoses to explain Harry's clinical presentation?

A Bullous impetigo

B Vesiculobullous tinea pedis

C Pompholyx eczema

D Epidermolysis bullosa simplex

E All of the above

Clinical presentation and differential diagnosis of EB

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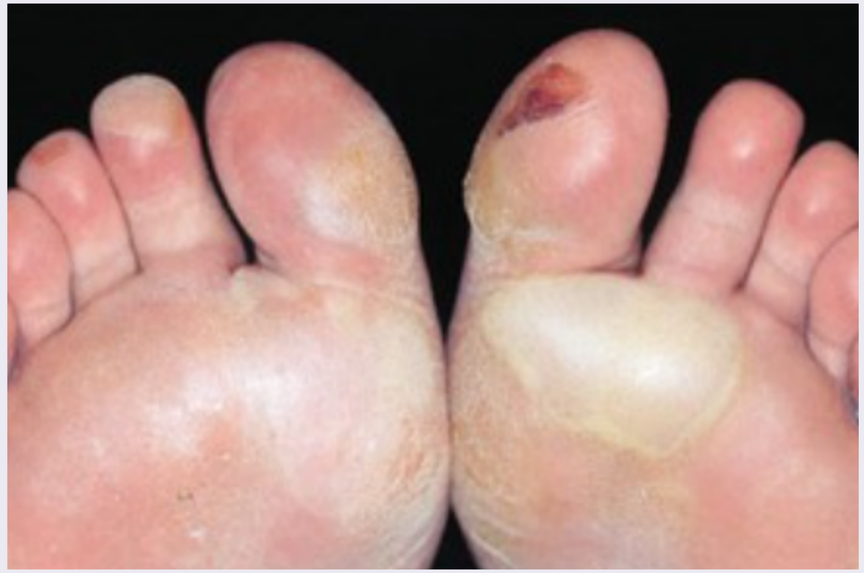

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QUESTION 1
CORRECT ANSWER!

Which of the following could be potential differential diagnoses to explain Harry's clinical presentation?

- ✗ Bullous impetigo
- ✗ Vesiculobullous tinea pedis
- ✗ Pompholyx eczema
- ✗ Epidermolysis bullosa simplex
- ✓ **All of the above**

CONTINUE

Clinical presentation and differential diagnosis of EB

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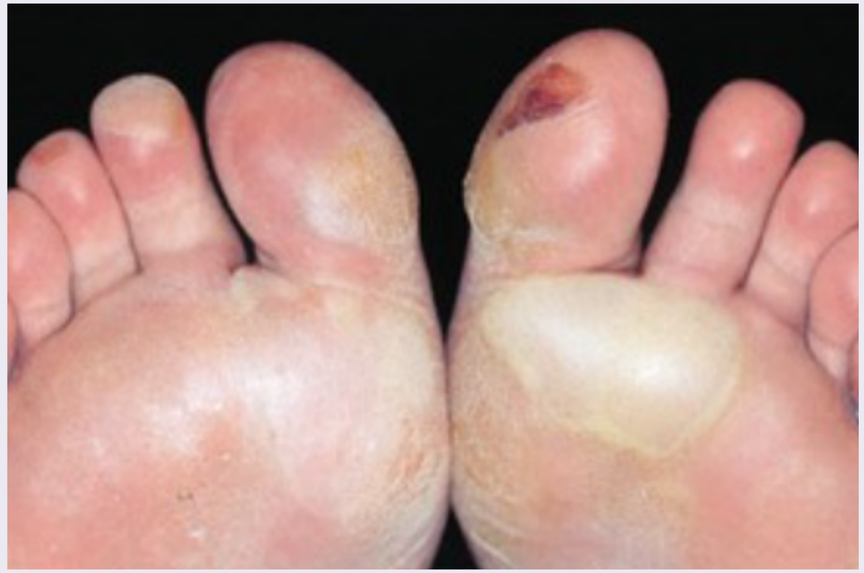

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QUESTION 1
INCORRECT, THE CORRECT ANSWER IS:

Which of the following could be potential differential diagnoses to explain Harry's clinical presentation?

- ✗ Bullous impetigo
- ✗ Vesiculobullous tinea pedis
- ✗ Pompholyx eczema
- ✗ Epidermolysis bullosa simplex
- ✓ **All of the above**

CONTINUE

Clinical presentation and differential diagnosis of EB

Click through the **tabs** to learn more about why each condition could be considered as a possible diagnosis for Harry.[1–4]

Bullous impetigo | Vesiculobullous tinea pedis | Pompholyx eczema | Epidermolysis bullosa simplex

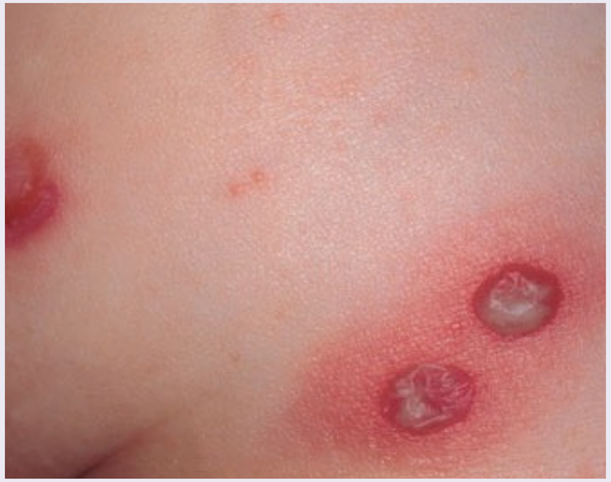
Nearly always caused by *Staphylococcus aureus*

Factors supporting Harry's diagnosis

- ✓ Localised blisters (bullae) present over a short period of time
- ✓ Distribution: bullous impetigo may involve the extremities (although the trunk is more frequently affected)

Factors not supporting Harry's diagnosis

- ? More common in children under the age of 2
- ? Usually asymptomatic or mildly pruritic; yet in Harry's case he experiences pain
- ? The bullae normally arise on erythematous skin
- ? When the bullae rupture, a honey-coloured crust can occur



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References

Clinical presentation and differential diagnosis of EB

Click through the **tabs** to learn more about why each condition could be considered as a possible diagnosis for Harry.[1–4]

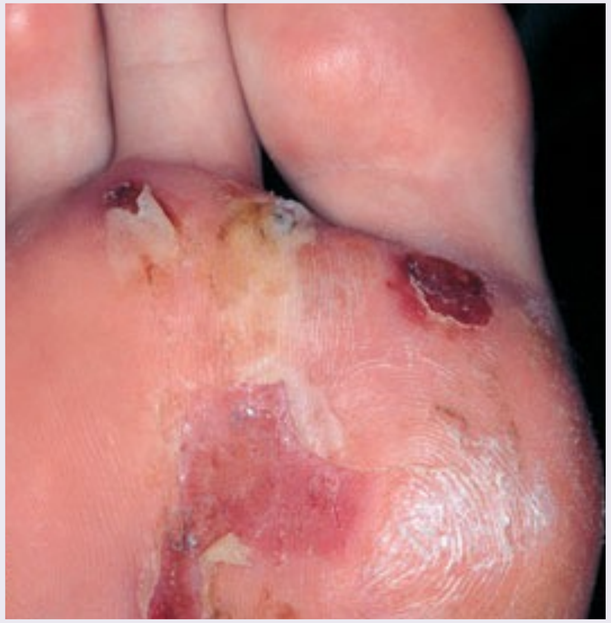
Bullous impetigo | **Vesiculobullous tinea pedis** | Pompholyx eczema | Epidermolysis bullosa simplex

Factors supporting Harry's diagnosis

- ✓ Usually occurs in teenagers and adults
- ✓ Vesicles or blisters affect the medial foot
- ✓ It may be painful

Factors not supporting Harry's diagnosis

- ? Often pruritic
- ? Underlying erythema is present alongside pruritic, dry or scaly maceration between the toes (with interdigital tinea pedis)
- ? No skin fragility is present



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Clinical presentation and differential diagnosis of EB

Click through the **tabs** to learn more about why each condition could be considered as a possible diagnosis for Harry.[1–4]

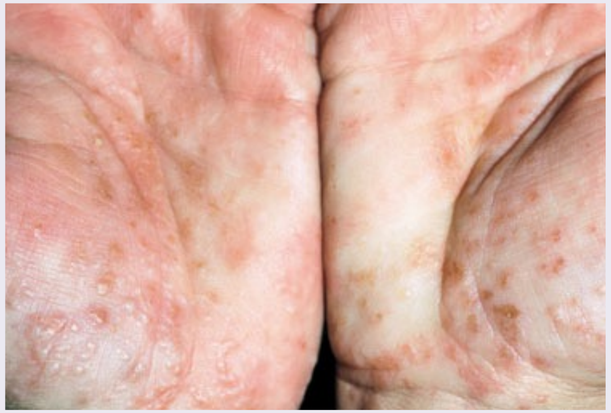
Bullous impetigo | Vesiculobullous tinea pedis | **Pompholyx eczema** | Epidermolysis bullosa simplex

Factors supporting Harry's diagnosis

- ✓ Vesicles can coalesce to form large bullae
- ✓ Occasionally the soles of the feet are affected

Factors not supporting Harry's diagnosis

- ? Incredibly pruritic, deep-seated vesicles, which mainly affect the palms and lateral aspects of the fingers are seen in pompholyx eczema
- ? Common in young adults
- ? Desquamation can occur
- ? No skin fragility is present



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References

Clinical presentation and differential diagnosis of EB

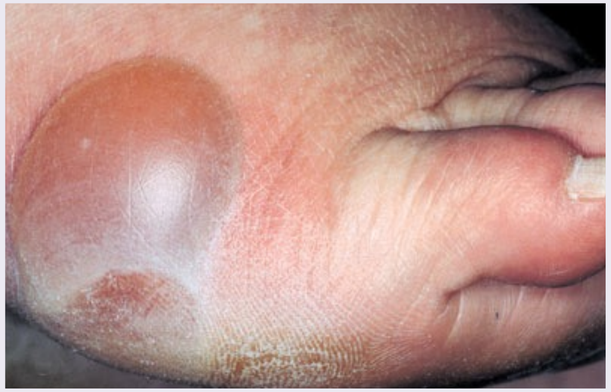
Click through the **tabs** to learn more about why each condition could be considered as a possible diagnosis for Harry.[1–4]

Bullous impetigo | Vesiculobullous tinea pedis | Pompholyx eczema | **Epidermolysis bullosa simplex**

Epidermolysis bullosa simplex (localised)

Factors supporting Harry's diagnosis

- ✓ Presents between infancy and the third decade of life
- ✓ Trauma or friction induced blisters mainly occur on the soles of the feet which heal without scarring



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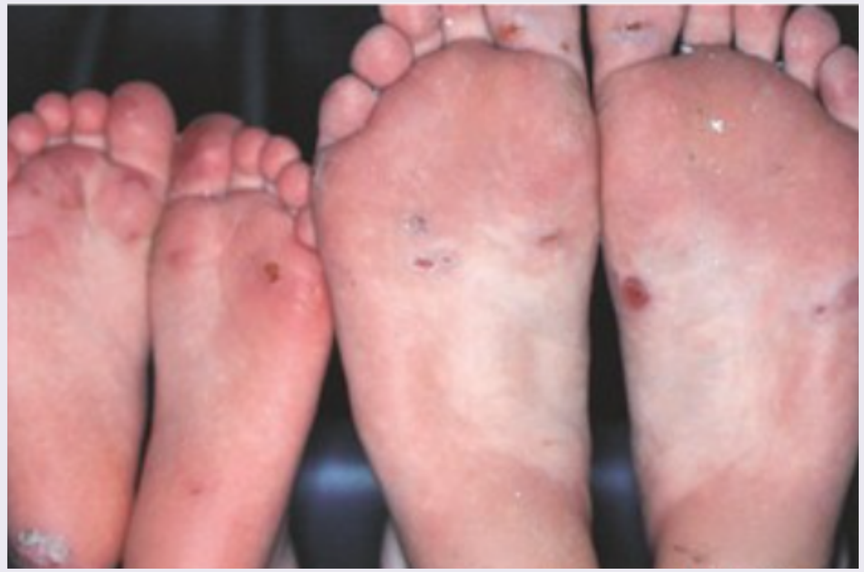
References

Clinical presentation and differential diagnosis of EB

Harry's mum, Samantha, reveals she has a very similar condition which affects her feet and she wonders if this is relevant.



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QUESTION 2

In light of these clinical findings in addition to the (suspected) positive family history which Samantha has just revealed, what is the most likely diagnosis for Harry?

A Bullous impetigo

B Vesiculobullous tinea pedis

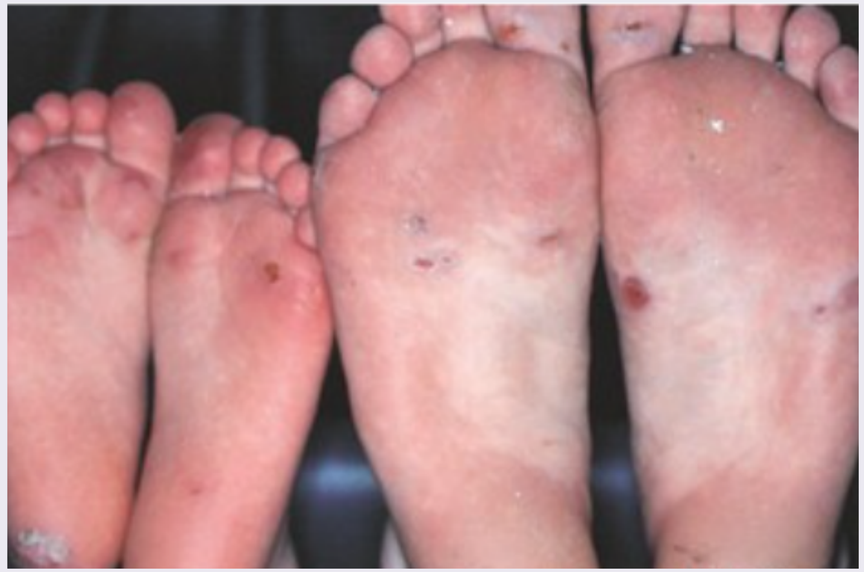
C Herpes simplex

D Pompholyx eczema

E Epidermolysis bullosa simplex

Clinical presentation and differential diagnosis of EB

Harry's mum, Samantha, reveals she has a very similar condition which affects her feet and she wonders if this is relevant.



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QUESTION 2
CORRECT ANSWER!

In light of these clinical findings in addition to the (suspected) positive family history which Samantha has just revealed, what is the most likely diagnosis for Harry?

- ✗ Bullous impetigo
- ✗ Vesiculobullous tinea pedis
- ✗ Herpes simplex
- ✗ Pompholyx eczema
- ✓ **Epidermolysis bullosa simplex**

Based on Harry's history, clinical findings and positive family history, the most likely diagnosis for Harry is *localised* epidermolysis bullosa simplex.

CONTINUE

Clinical presentation and differential diagnosis of EB

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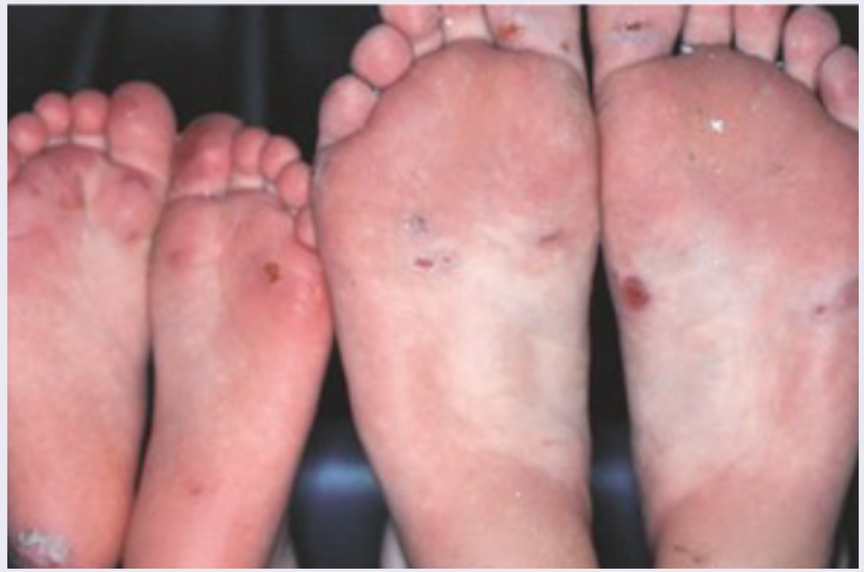

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- ✗ Vesiculobullous tinea pedis
- ✗ Herpes simplex
- ✗ Pompholyx eczema
- ✓ **Epidermolysis bullosa simplex**

Based on Harry's history, clinical findings and positive family history, the most likely diagnosis for Harry is *localised* epidermolysis bullosa simplex.

CONTINUE

Clinical presentation and differential diagnosis of EB (1 of 2)

There are several differential diagnoses to consider and exclude when reviewing patients with suspected EB.[5–13]
For this reason, it is important to understand how to differentiate the diagnoses from EB and what investigations to undertake.

Differential diagnosis	How to differentiate this diagnosis from EB	Investigations
Bullous impetigo	• Tense blisters arise on erythematous skin in a localised distribution, which rupture and form a honey-coloured crust • The skin is not mechanically fragile (unlike in EB)	• Clinical diagnosis • Consider taking a swab for MC&S in recurrent or treatment resistant cases
Vesiculobullous tinea pedis	• Interdigital erythema and maceration (interdigital tinea pedis) and vesicles/blisters are seen with vesiculobullous tinea pedis	• Consider skin scrapings for mycology
Pompholyx eczema	• Incredibly pruritic vesicular lesions affecting the palms, lateral aspects of the fingers and sometimes the feet, are key features of pompholyx eczema. In severe cases, large bullae (blisters) may develop on these areas	• Clinical diagnosis
Herpes simplex	• Although lesions can be painful they are usually vesicular lesions instead of bullae (unlike EB) • Distribution differs to EB with (HSV-1) herpes simplex virus affecting the face and HSV-2 affecting the genital area • There are no other EB findings, i.e., the skin is not mechanically fragile	• Clinical diagnosis • If there is diagnostic uncertainty, consider taking a viral swab
Staphylococcal scaled skin syndrome (SSSS) *(SSSS is caused by exotoxins of strains of Staphylococcus aureus)*	• Usually affects young children • Presents with generalised painful erythema erosions, superficial blisters and desquamation • Unlike in EB, the child is unwell with fever, malaise etc., and in SSSS Nikolsky sign (where the skin separates at the epidermis on stroking) is positive	• Consider a swab for MC&S to confirm the presence of *S. aureus* • Consider a skin biopsy in challenging cases
Non-accidental injury (NAI)	• The erosions/wounds from burns or injuries have a variable depth within the same lesion (unlike EB where they are all the same depth)	• Refer directly to paediatrics for a same day assessment as well as referring to your local safeguarding team

References

Clinical presentation and differential diagnosis of EB (2 of 2)

There are several differential diagnoses to consider and exclude when reviewing patients with suspected EB.[5–13]
For this reason, it is important to understand how to differentiate the diagnoses from EB and what investigations to undertake.

Differential diagnosis	How to differentiate this diagnosis from EB	Investigations
Epidermolysis bullosa acquisita (EBA)	• This is a separate disorder from EB and classified as an immunobullous disorder with an autoimmune component • It can resemble dystrophic EB with bullae (and vesicles) arising at the site of trauma which heal with milia, scarring and hyperpigmentation • This rare autoimmune immunobullous condition does not fall within the EB definition	• Autoimmune serology can be considered as 50% have IgG autoantibodies targeting the basement membrane • 2x skin biopsies from an intact blister and peri-lesional skin for direct immunofluorescence
Other immunobullous diseases including: • Bullous pemphigoid (BP) • Pemphigus vulgaris (PV) • Pemphigus foliaceus (PF) • Linear IgA disease	• These conditions are rare in newborns (although neonatal PV can be acquired transplacentally) • The distribution of blisters may differ from EB although both can be pruritic • The skin is not mechanically fragile in immunobullous disorders and they often lack the other features associated with EB including milia, scarring and nail dystrophy	• 2x skin biopsies from an intact blister and peri-lesional skin for direct immunofluorescence • Autoimmune serology including pemphigoid and pemphigus antibodies (and desmoglein-1 antibodies in PF)
Congenital porphyria	• Photosensitivity with vesicles, blisters, scarring and milia (unlike in EB the skin is not markedly fragile)	• Consider testing for serum/urine/faecal porphyrins • Consider a skin biopsy
Bullous mastocytosis	• Skin coloured/yellow nodules/plaques which can form tense blisters with friction • They may be induced by gentle contact/stroking of the skin (Darier's sign) • No skin fragility, scarring or nail dystrophy are present unlike in EB	• This can be a clinical diagnosis but if there is uncertainty a skin biopsy may be considered • Consider measuring serum tryptase
Epidermolytic ichthyosis	• Erythroderma, blistering and loss of skin present from birth which is then replaced by a thick hyperkeratotic scale (unlike in EB the skin is not markedly fragile)	• Skin biopsy and genetic testing

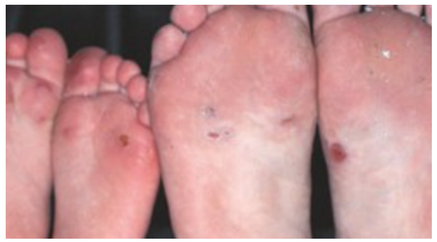
References

Clinical presentation and differential diagnosis of EB

Although there are several types of EB, each with their own hallmark symptoms and signs, the characteristic clinical features suggestive of EB may include the following:[14]

- Mechanically **fragile skin**
- Trauma of **friction-induced blisters**
- **Scarring and/or milia** may be present depending on the type of EB
- **Nail involvement** and/or scarring alopecia may be seen in some types/sub-types of EB
- **Multisystem extracutaneous involvement** is also a feature of some types of EB
- The **presentation of EB** can vary depending on its type/subtype, ranging **from birth to the third decade of life**, though this late-onset is uncommon. For instance, dystrophic EB will present from birth, yet localised EB simplex may present between infancy and the third decade of life

You will learn about more about **different types of EB** later in this module.



References

Clinical presentation and differential diagnosis of EB

It is important to remember that when we see and examine patients with lesions which have the characteristic features of EB, we need to ask ourselves the following question:[14]

Can we exclude EB from our list of differential diagnoses?

- **Yes**
- **No**

If we cannot exclude EB from our list of differential diagnoses, we need to **refer to secondary care** to confirm the diagnosis

You will learn about the **referral process** later in this module.

References

Now, let’s learn about the EB stats...

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   Blistered feet and pain while playing football

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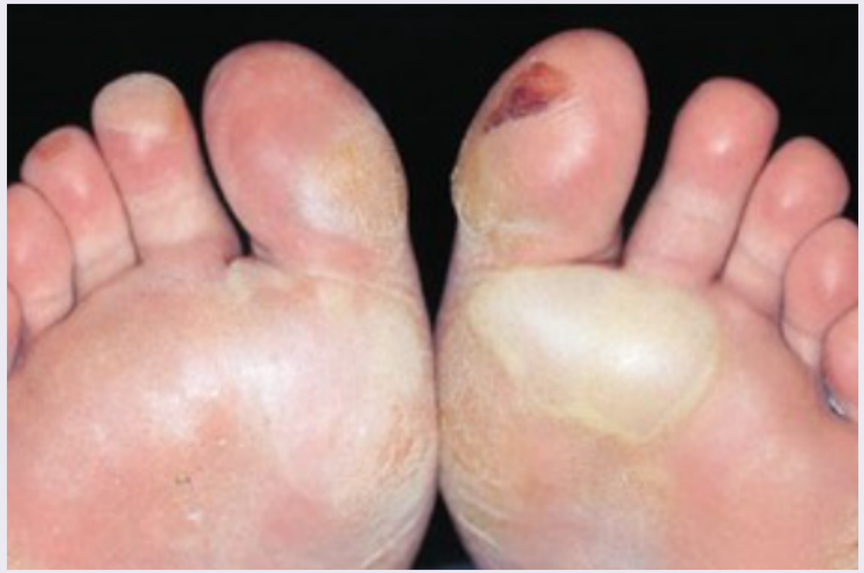
Epidemiology of EB

Our working diagnosis for Harry is EB.



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QUESTION 3

Which one of the following statements regarding EB is true?

A EB is an autoimmune immunobullous disorder

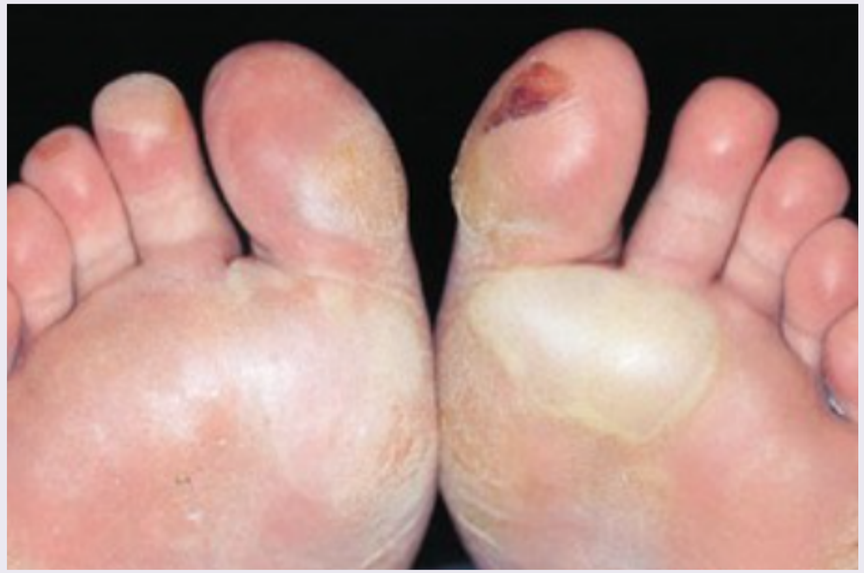
B The only known risk factor for EB is having a positive family history

C EB is more common in women

D There are five major classic types of EB

Epidemiology of EB

Our working diagnosis for Harry is EB.



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CORRECT ANSWER!

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- ✓ **The only known risk factor for EB is having a positive family history**
- ✗ EB is more common in women
- ✗ There are five major classic types of EB

CONTINUE

Epidemiology of EB

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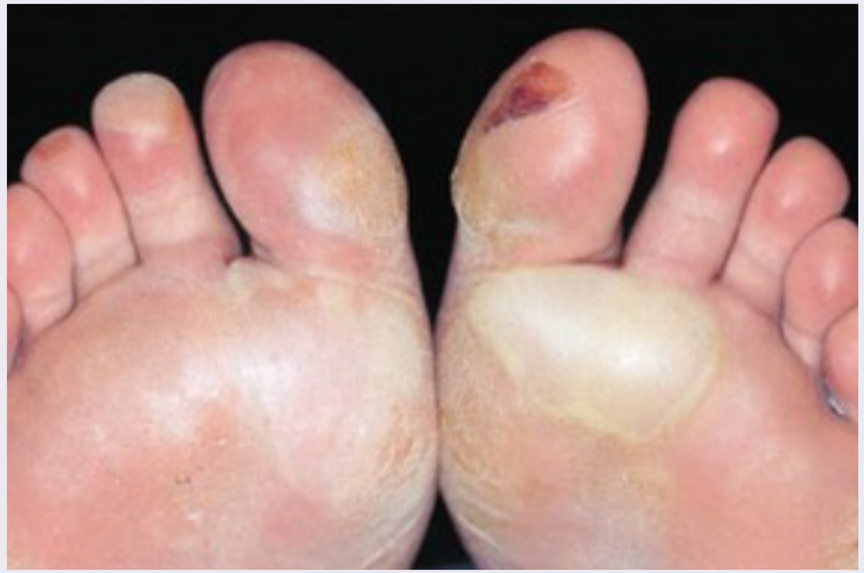

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QUESTION 3

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Which one of the following statements regarding EB is true?

- ✗ EB is an autoimmune immunobullous disorder
- ✓ **The only known risk factor for EB is having a positive family history**
- ✗ EB is more common in women
- ✗ There are five major classic types of EB

CONTINUE

Epidemiology of EB

Prevalence in USA: 11.1 per 1 million[15]

USA National EB Registry of 3300 people (collected between 1986–2002)

Prevalence in UK: 15–35 cases per 1 million[16]

Prevalence in Scotland: 49 cases per 1 million[8,17]

No differences were seen in the prevalence of EB between different genders or ethnic groups.[8]

These figures are likely to be an underestimate as certain less severe forms of EB (i.e., EBS) may be underdiagnosed.[4,8]

References

Epidemiology of EB

EB currently includes **4 major classic types** (which have at least 30 clinical phenotypes):[6–8,14,17]

Type of EB	Prevalence	Location of fragility due to defective structural proteins	Inheritance pattern
EB simplex (EBS)	70% of all cases	Epidermis	Usually inherited in an autosomal dominant (AD) pattern, although de novo (new) mutations can occur in ~30% of cases
Dystrophic EB (DEB)	25% of all cases	Papillary dermis	Inherited either in an AD or autosomal recessive (AR) pattern depending on the subtype
Junctional EB (JEB)	5% of all cases	Dermal-epidermal junction/ basement membrane	Inherited in an AR pattern
Kindler EB (KEB)	Rare	Variable levels of ultrastructural splits within the basement membrane zone	Inherited in an AR pattern

References

Epidemiology of EB

In EB, **mutations** occur within genes that encode and give rise to **mechanical disruption in specific structural proteins**, resulting in interference of cell adhesion, tissue barrier and repair functioning which can lead to **cell and tissue dehiscence**.[7,8,17]

The affected structural proteins determine the site of blistering for each of the subtypes:[7,8]

- **EB simplex** — the epidermis is affected
- **Junctional EB** — the dermal-epidermal junction is affected
- **Dystrophic EB** — the papillary dermis is affected

EB is therefore **classified** by the following:[6,8]

- Ultra-structural level of fragility where the blisters occur
- Clinical phenotype
- Genotype

The **only known risk factor** for EB is having a **positive family history**, it is, therefore, **crucial we establish** if this is known during our consultations.[6]

References

How is EB classified?

Classification of EB

We suspect Harry has EB simplex, which is the most common type of EB.

It is important to acknowledge that its true prevalence is unknown, as it is likely to remain undiagnosed in many cases.

QUESTION 4

What is one of the most common symptoms patients with EB simplex present with?

A Pruritus

B Secondary bacterial infection

C Allodynia

D Paraesthesia

Classification of EB

We suspect Harry has EB simplex, which is the most common type of EB.

It is important to acknowledge that its true prevalence is unknown, as it is likely to remain undiagnosed in many cases.

QUESTION 4
CORRECT ANSWER!

What is one of the most common symptoms patients with EB simplex present with?

- [x] **Pruritus**
- [ ] Secondary bacterial infection
- [ ] Allodynia
- [ ] Paraesthesia

In Harry's case, EB simplex (EBS) is characterised by pruritus (one of the most common symptoms), neuropathic pain, tissue fragility, inflammation and a potential failure to thrive.[8,18]

CONTINUE

Classification of EB

We suspect Harry has EB simplex, which is the most common type of EB.

It is important to acknowledge that its true prevalence is unknown, as it is likely to remain undiagnosed in many cases.

QUESTION 4

INCORRECT, THE CORRECT ANSWER IS:

What is one of the most common symptoms patients with EB simplex present with?

- [x] **Pruritus**
- [ ] Secondary bacterial infection
- [ ] Allodynia
- [ ] Paraesthesia

In Harry's case, EB simplex (EBS) is characterised by pruritus (one of the most common symptoms), neuropathic pain, tissue fragility, inflammation and a potential failure to thrive.[8,18]

CONTINUE

Classification of EB

The initial presentation of EB usually **occurs at birth or in early infancy**, occasionally some cases of localised EB simplex (EBS) may be mild enough to remain undetected until later life.[8,18]

Depending on the location of the molecular and structural defect, classic hallmarks of EB can include the following:[8,19]

- Mechanically fragile skin
- Peeling
- Erosions
- Blisters
- Ulceration
- Wounds
- Atrophic scars

Extracutaneous clinical features of EB can also be present, which can result in multisystem involvement.[8,19]

Clinical diagnosis of EB can be difficult during the early stages, particularly without an established family history of EB.[8]

Classification of EB

In this section you will learn more about the 4 classic types of EB and their symptoms:[14]

EB simplex (EBS)

The **most common form** of EB, EBS causes **blistering in the upper layers** of the skin, often **triggered by friction or minor trauma**.

Dystrophic EB (DEB)

In DEB, **blistering occurs deeper in the skin** and can lead to scarring and **long-term damage**, especially around **joints and limbs**.

Junctional EB (JEB)

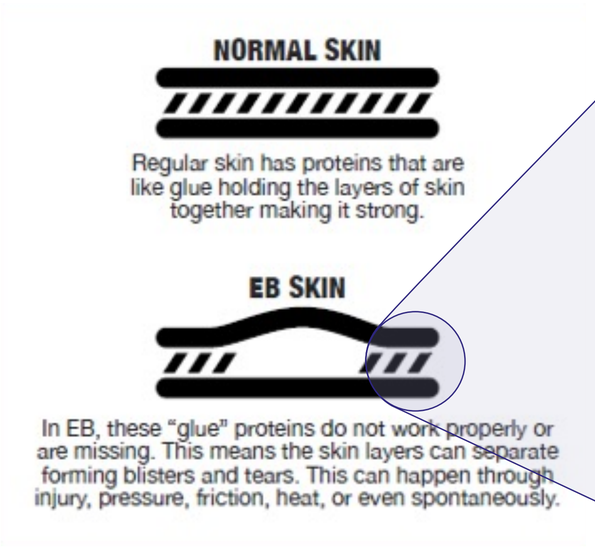
A **rarer** but often **more severe type**, JEB involves blistering at the level where the **outer and inner layers of skin** meet and can affect **internal linings**.

Kindler EB (KEB)

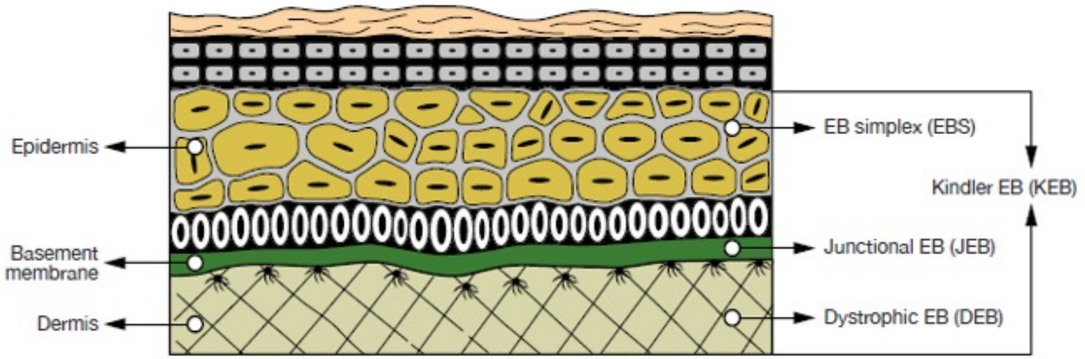
The **rarest form** of EB, KEB combines **features of multiple EB types**, with blistering that may occur at **different skin depths** and **photosensitivity**.

HOW DOES EB AFFECT THE SKIN?

How EB affects the different layers of the skin[20]



Cross-section diagram of the skin



DEBRA International - adapted from Debra of America and the US National Institute of Arthritis and Musculoskeletal and Skin Disease

Frequency and classification of EB types

Classification of EB: **EB simplex (EBS)**

The most common type of EB.[15,19]

Characterised by the following symptoms:[8,21,22]

- Pruritus and pain (possibly with neuropathic characteristics) – **the most common symptoms**
- Tissue fragility
- Inflammation
- Potential failure to thrive (in young children with severe EBS)

There are **many different subtypes** of EBS, the most common subtypes are:[4,17,19]

- Localised EBS
- Intermediate EBS
- Severe EBS

MORE ABOUT EBS SUBTYPES

EBS has a **broad spectrum of clinical manifestations** ranging from **minor blistering of the feet** (occurring within the epidermis) following frictional trauma through to **extracutaneous involvement**. In **rare** cases, this may include the involvement of theoesophagus or larynx, which may prove **fatal for some patients**.[6,8,17,19]

Common subtypes of EBS[4,17,19]

Subtype of EBS	Demographic	Clinical features	Important features to note
Localised EBS	Presents between infancy and the third decade of life	• Trauma or friction-induced blisters mainly occur on the soles of the feet • ~10% of patients have blisters at other sites, including the palms, neck, waist, knees (in children when they are crawling) • Blisters usually heal without scarring	• The blisters are often induced by friction from clothing and physical activity • Blisters occur more commonly in warm weather • Palmoplantar hyperhidrosis is commonly associated with localised EBS
Intermediate EBS	Presents at birth or within the first year of life	• Trauma or friction induced blisters which are more widespread affecting the hands, feet, back, legs and occipital area	• Unlike localised EBS, 60% of patients will have localised scarring and 15% have milia
Severe EBS	Presents at birth	• Severe and extensive blisters involve the palms, soles, mucous membranes, trunk, limbs and neck, with a classic annular or herpetiform pattern to the blisters • Post-inflammatory hyperpigmentation is common, and 40% of cases have localised atrophic scarring	• Hyperkeratosis on the palms and soles can develop into a keratoderma, which is common in childhood • Nail dystrophy and nail shedding are often seen • DEBRA reminds us how this can be fatal during the first year of life

Classification of EB: **Dystrophic EB (DEB)**

There are two subtypes of dystrophic EB (DEB) depending on how the condition is inherited.[6]

Click on each **tab** to learn more about each subtype.

Autosomal dominant dystrophic EB (DDEB) | Autosomal recessive dystrophic EB (RDEB)

The characteristic and hallmark clinical features of DDEB include:

- **Skin fragility, blistering** from birth or early infancy (which often affects the acral and bony prominences, i.e., elbows/knees) followed by scarring and milia[4,8,19]
- **Nail dystrophy** is common[19]
- **Hyperkeratosis** of the digits, extremities and limbs may cause **flexion contractures**[19]

Generally, **RDEB is more severe** than DDEB, although there are subtypes of both which vary phenotypically.[6,19]

Classification of EB: **Dystrophic EB (DEB)**

There are two subtypes of dystrophic EB (DEB) depending on how the condition is inherited.[6]

Click on each **tab** to learn more about each subtype

Autosomal dominant dystrophic EB (DDEB) | **Autosomal recessive dystrophic EB (RDEB)**

RDEB also has several subtypes which differ in their clinical appearance, with severe RDEB presenting with:[4,8,17,18]

- **Pruritus** and **intense pain**
- **Skin fragility** with **widespread blisters** from birth
- **Absence of skin at birth** (especially the lower legs, often due to birth trauma)
- **Extensive atrophic scarring** (or occasionally **hypertrophic scarring**)
- Increased risk of **secondary infection** at the wound site
- **Multisystem extracutaneous involvement** can occur, including perianal lesions, resulting in constipation, scarring alopecia, microstomia and ocular complications
- **Oesophageal stricture** (causing acute pain and dysphagia, particularly for solids) can lead to chronic malnutrition and many patients are short in stature, flexion contractions of limbs, and pseudosyndactyly
- **Localised RDEB** can manifest as **late-onset disease** in adulthood where **skin fragility and blisters** (+/- nail involvement) are often **limited to acral sites**

Generally, **RDEB is more severe** than DDEB, although there are subtypes of both which vary phenotypically.[6,19]

Classification of EB:
Dystrophic EB (DEB)

Generally, **RDEB is more severe** than DDEB, although there are subtypes of both which vary phenotypically.[6,19]

Patients with **RDEB** are also at a **very high risk** of the wound site transforming into an **aggressive squamous cell carcinoma** (SCC) — even in individuals as young as 6 years of age, though this is very rare in childhood.[8,17,18]

SCCs are the leading cause of death in patients with RDEB.[8,18]

These photos have been shared by DEBRA to highlight the **clinical presentation** of **RDEB.**

A patient with **pseudosyndactyly**, which occurs with **fusion of adjacent fingers and toes** due to blisters and scarring. The digits can undergo progressive contractures, which become encased in scar tissue, known as **mitten deformity.**[8,17,18]

Classification of EB

Now that you have covered dystrophic EB (DEB), take a moment to answer this question.

QUESTION 5

Which of the following is ***not*** a characteristic cutaneous feature of dystrophic EB?

A Intense pain and pruritus

B Skin fragility

C Hyperpigmentation

D Nail dystrophy

E Widespread blisters from birth

Classification of EB

Now that you have covered dystrophic EB (DEB), take a moment to answer this question.

QUESTION 5
CORRECT ANSWER!

Which of the following is ***not*** a characteristic cutaneous feature of dystrophic EB?

- ☒ Intense pain and pruritus
- ☒ Skin fragility
- ☑ **Hyperpigmentation**
- ☒ Nail dystrophy
- ☒ Widespread blisters from birth

Hyperpigmentation is *not a classic hallmark feature* of dystrophic EB.

CONTINUE

Classification of EB

Now that you have covered dystrophic EB (DEB), take a moment to answer this question.

QUESTION 5

INCORRECT, THE CORRECT ANSWER IS:

Which of the following is ***not*** a characteristic cutaneous feature of dystrophic EB?

- ✗ Intense pain and pruritus
- ✗ Skin fragility
- ✓ **Hyperpigmentation**
- ✗ Nail dystrophy
- ✗ Widespread blisters from birth

Hyperpigmentation is *not a classic hallmark feature* of dystrophic EB.

CONTINUE

Classification of EB: **Junctional EB (JEB)**

An autosomal recessive disorder where the hallmark feature of blistering **affects the basement membrane**.[8]

There are **several variants** of JEB, the most common of which include **intermediate JEB** and **severe JEB**.[8,17]

Characterised by the following symptoms:

- Mechanical fragility of the skin[6,17,19]
- Recurrent blisters (which are often mild and localised at birth but rapidly progress into generalised, extensive mucocutaneous blistering)
- Erosions
- Poor wound healing
- Over-granulation of the tissue

All patients with JEB have dental enamel defects ranging from pitting to hypoplasia.[4,6,19]

In severe JEB:

- **Skin is extremely fragile** and even being lifted as a baby may cause extensive blistering[19]
- Often features a **hoarse cry**[23]
- Often **fatal** within the first 24 months of life[6,8,19]

The clinical presentation of **intermediate JEB** is less severe, although there is an **elevated SCC risk** in adulthood.[6,17]

Some patients with JEB will experience further **extracutaneous involvement** with the presence of any of the following:[4,6,19]

- Nail dystrophy
- Pyloric atresia
- Trachea or laryngeal stenosis/strictures
- Severe upper airway disease

Classification of EB: **Kindler EB (KEB)**

A **rare subtype** of EB which is inherited in an **autosomal recessive pattern**.[8]

It presents from **birth or early childhood** with the following features:[6,8,19]

- Skin fragility
- Generalised blistering
- Photosensitivity

In most cases, as the **child ages** the blistering reduces but is replaced by:[8,17]

- Poikiloderma with hyper-/hypopigmentation changes
- Skin atrophy
- Mucocutaneous scarring
- Progressive palmoplantar keratoderma

Extracutaneous symptoms can include:[8]

- Gingivitis
- Dental disease
- Colitis
- Oesophageal narrowing
- Urethral strictures

SCCs have been reported to predominantly affect the **acral or mucosal sites**.[8]

Classification of EB: **Kindler EB (KEB)**

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Classification of EB: Practical resources

Here are some additional resources to help you in your clinical practice:

- **DEBRA summary of EBS**
- **DermNet overview of EBS** – includes some useful reference images of different types of EB
- C Has *et al. BJD*. 2020;183(4):614–627, **https://doi.org/10.1111/bjd.18921** – includes some useful reference images of different types of EB
- **DEBRA summary of DEB**
- **DEBRA summary of JEB**
- **DEBRA summary of KEB**

Classification of EB

Before moving on to the next section, take a minute to think about this question.

QUESTION 6

Which of the following sites is involved in all patients with junctional EB?

A Dental involvement

B Hepatobiliary involvement

C Cardiovascular involvement

D Respiratory involvement

Classification of EB

Before moving on to the next section, take a minute to think about this question.

QUESTION 6

CORRECT ANSWER!

Which of the following sites is involved in all patients with junctional EB?

- [x] **Dental involvement**
- [ ] Hepatobiliary involvement
- [ ] Cardiovascular involvement
- [ ] Respiratory involvement

All patients with junctional EB (JEB) have dental enamel defects ranging from pitting to hypoplasia.

CONTINUE

Classification of EB

Before moving on to the next section, take a minute to think about this question.

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INCORRECT, THE CORRECT ANSWER IS:

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- ✓ **Dental involvement**
- ✗ Hepatobiliary involvement
- ✗ Cardiovascular involvement
- ✗ Respiratory involvement

All patients with junctional EB (JEB) have dental enamel defects ranging from pitting to hypoplasia.

CONTINUE

How can you refer a patient with suspected EB?

1. **Clinical presentation and differential diagnosis of EB**
   Blistered feet and pain while playing football
2. **Epidemiology of EB**
   Establishing the family history with mum, Samantha
3. **Classification of EB**
   Determining the type of EB Harry has
4. **Referral to an EB centre**
   Harry and his mum are referred for accurate further care
5. **Confirming the diagnosis and management**
   Both receive precise diagnoses with expert support and management of symptoms

Referring patients with EB

Returning to our consult with Harry and his mum, Samantha.

We are fairly confident they both have localised EB simplex.

Take a minute to answer this question regarding the appropriate next steps to take.

QUESTION 7

What is the most appropriate next step to confirm this diagnosis for both Harry and Samantha?

A Make a clinical diagnosis of localised EBS and manage this condition in primary care

B Refer to your local dermatology department

C Refer to your genetics colleagues

D Refer to a designated EB Centre of Excellence

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CORRECT ANSWER!

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- ☒ Refer to your local dermatology department
- ☒ Refer to your genetics colleagues
- ☑ **Refer to a designated EB Centre of Excellence**

For all patients suspected of having EB, it is essential they are reviewed by a dermatologist experienced in the diagnosis and management of EB.

CONTINUE

Referring patients with EB

Returning to our consult with Harry and his mum, Samantha.

We are fairly confident they both have localised EB simplex.

Take a minute to answer this question regarding the appropriate next steps to take.

QUESTION 7

INCORRECT, THE CORRECT ANSWER IS:

What is the most appropriate next step to confirm this diagnosis for both Harry and Samantha?

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- ☒ Refer to your genetics colleagues
- ☑ **Refer to a designated EB Centre of Excellence**

For all patients suspected of having EB, it is essential they are reviewed by a dermatologist experienced in the diagnosis and management of EB.

CONTINUE

Referring patients with EB

If you suspect a patient has EB, you are recommended to refer directly to a **designated EB Centre of Excellence**.[6]

These centres provide specialist EB expertise to ensure a **precise diagnosis** is made, and patients receive the **care and support** they need.[14,18]

EB Centres of Excellence[14]

For adults

- Glasgow Royal Infirmary
- Solihull Hospital
- Guy's and St Thomas' Hospital

For children

- Glasgow Royal Hospital for Children
- Birmingham Women's and Children's Hospital
- Great Ormand Street Children's Hospital

Referring patients with EB

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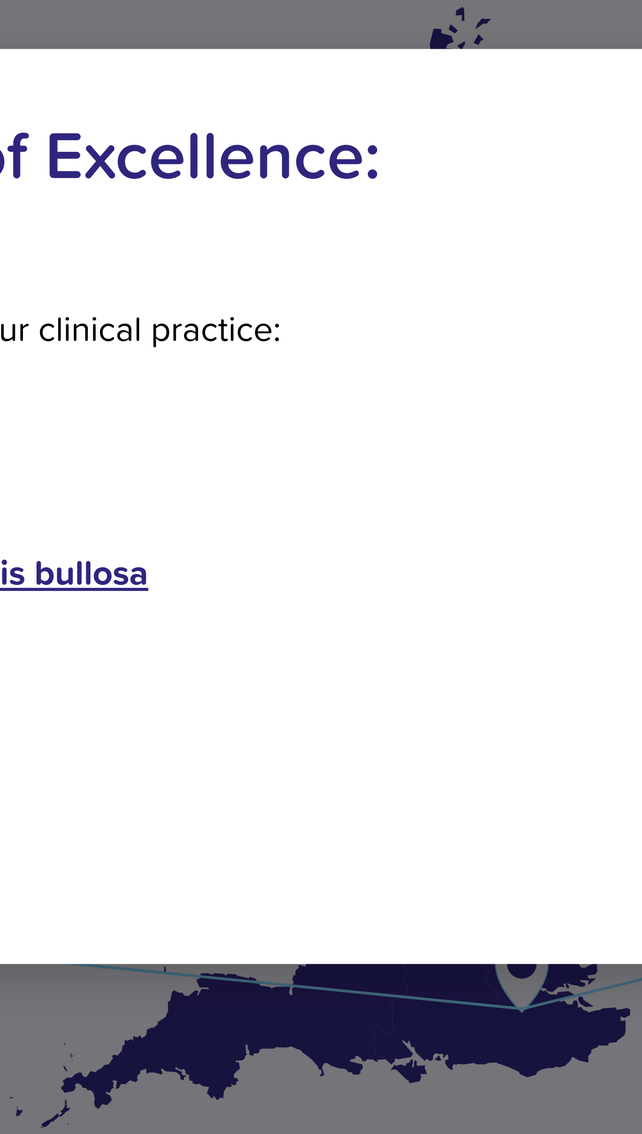
EB Centres of Excellence[14]



St Thomas' Hospital

Children's Hospital

Referring to an EB Centre of Excellence: Practical resources

Here are some additional resources to help you in your clinical practice:

- **BMJ Best Practice: Epidermolysis bullosa**
- **DEBRA: Accessing specialist care for EB**
- **Primary Care Dermatology Society: Epidermolysis bullosa**

Finally, let’s learn about what happens after diagnosis...

Clinical presentation and differential diagnosis of EB
Blistered feet and pain while playing football

Epidemiology of EB
Establishing the family history with mum, Samantha

Classification of EB
Determining the type of EB Harry has

Referral to an EB centre
Harry and his mum are referred for accurate further care

5

Confirming the diagnosis and management
Both receive precise diagnoses with expert support and management of symptoms

Diagnosis and management of EB

Thinking back to Harry and his mum Samantha, they are both referred to their EB Centre of Excellence.

Subsequently, they are both diagnosed with localised EBS.

QUESTION 8

Consider whether the following statement is **true** or **false**:

‘Management of EB is offered by specialist multidisciplinary teams who aim to offer symptomatic therapies to try to improve the debilitating pain and pruritus which can be associated with EB, as well as promoting wound healing and trying to reduce complications.’

A True

B False

Diagnosis and management of EB

Thinking back to Harry and his mum Samantha, they are both referred to their EB Centre of Excellence.

Subsequently, they are both diagnosed with localised EBS.

QUESTION 8
CORRECT ANSWER!

Consider whether the following statement is **true** or **false**:

‘Management of EB is offered by specialist multidisciplinary teams who aim to offer symptomatic therapies to try to improve the debilitating pain and pruritus which can be associated with EB, as well as promoting wound healing and trying to reduce complications.’

- [x] **True**
- [ ] False

CONTINUE

Diagnosis and management of EB

Thinking back to Harry and his mum Samantha, they are both referred to their EB Centre of Excellence.

Subsequently, they are both diagnosed with localised EBS.

QUESTION 8

INCORRECT, THE CORRECT ANSWER IS:

Consider whether the following statement is **true** or **false**:

‘Management of EB is offered by specialist multidisciplinary teams who aim to offer symptomatic therapies to try to improve the debilitating pain and pruritus which can be associated with EB, as well as promoting wound healing and trying to reduce complications.’

- [x] **True**
- [ ] False

CONTINUE

Diagnosis and management of EB: Diagnostic approach

The following approach is used by EB Centres of Excellence to confirm a diagnosis of EB:[6,8,14]

- **Take a comprehensive detailed history**
- **Conduct a focused clinical examination** to identify the hallmark characteristic cutaneous and extracutaneous features of EB
- **Establish if a family history exists** (consider that some cases can arise de novo)

EB is a **secondary care diagnosis** where the ultrastructural level within which blisters develop is established by taking a **skin biopsy** from a fresh blister.[5,6,19]

EB is then **further classified** on the following:[5,6,19]

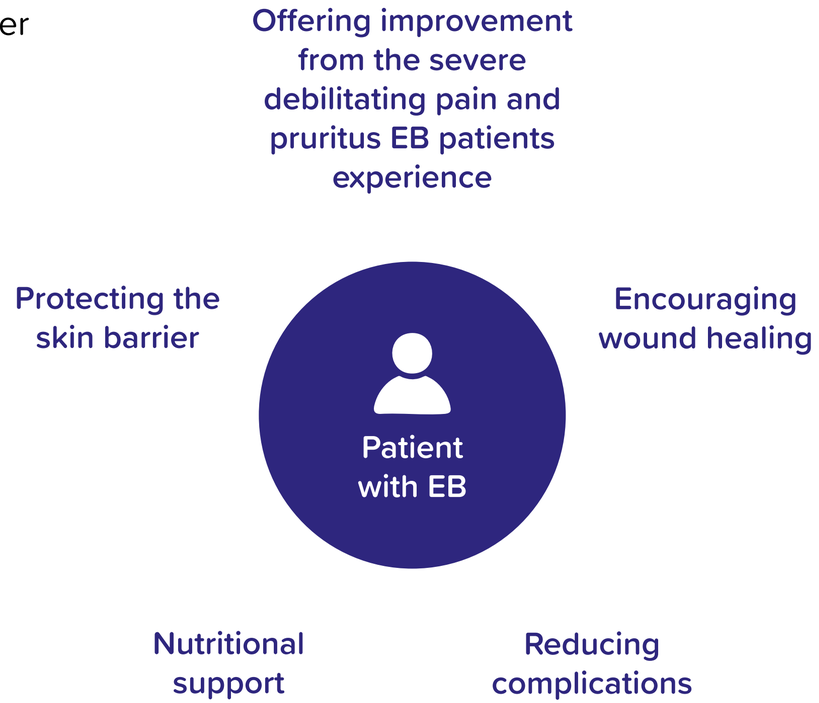
- Immunohistochemistry
- Mutational analysis
- Clinical phenotype

Clinical acumen is crucial and by referring suspected EB cases to the expert designated EB Centres this will allow accurate EB diagnoses to be established.[14]

References

Diagnosis and management of EB: Management approach

Management is achieved with **supportive care** provided by **multidisciplinary teams** who offer **symptomatic therapies** aimed at:[4,6,18,24]



To date, there is **no curative treatment** for any EB subtype.[4,18]

Management is directed towards improving functionality and patient wellbeing.

Before we finish...

Now you have completed this learning module,
please take this quiz again to check your knowledge.

Click the button below to start the post-learning quiz.

START THE QUIZ

Remember, the quiz is not timed, so take the time you need to complete it.

Compare your score now to the beginning of the module — are there any areas you would like to revisit?

You can access other useful resources on EB by visiting the DEBRA website.

Congratulations

You have now completed this learning module on epidermolysis bullosa (EB).

We hope you feel more confident in your understanding of EB.

Please complete the **feedback form** to share your thoughts and help shape future modules.

How to put this learning into practice

- **Audit** your practice list to see if you have any patients coded with a diagnosis of EB
  - If so, check they are under the **care of an EB Centre of Excellence**
- Use this **link** to ensure you know **how to refer** your patients with suspected EB to your closest EB Centre of Excellence

References

References

1. Society PCD. Impetigo. Primary Care Dermatology Society. 2022. Available at: www.pcds.org.uk/clinical-guidance/impetigo. Accessed June 2025.
2. UpToDate. Dermatophyte (tinea) infections. Available at: www.uptodate.com/contents/dermatophyte-tinea-infections. Accessed June 2025.
3. DermNet. Dyshidrotic eczema (Pompholyx, Vesicular Hand Eczema). 2024. Available at: https://dermnetnz.org/topics/dyshidrotic-eczema. Accessed June 2025.
4. Griffiths CEM *et al. Rook's Textbook of Dermatology: Genetic Blistering Diseases*. John Wiley & Sons: New Jersey, 2024.
5. UpToDate. Diagnosis of epidermolysis bullosa. Available at: www.uptodate.com/contents/diagnosis-of-epidermolysis-bullosa. Accessed June 2025.
6. BMJ Best Practice. Epidermolysis bullosa - Symptoms, diagnosis and treatment. Available at: https://bestpractice.bmj.com/topics/en-gb/744. Accessed June 2025.
7. Bolognia JL, *et al. Dermatology*. 4th ed. Elsevier: Philadelphia, 2018.
8. Bardhan A, *et al. Nat Rev Dis Primers*. 2020;6(1):1–27.
9. Society PCD. Herpes simplex. Primary Care Dermatology Society. 2023. Available at: www.pcds.org.uk/clinical-guidance/herpes-simplex. Accessed June 2025.
10. UpToDate. Staphylococcal scaled skin syndrome (SSSS). 2024. Available at: www.uptodate.com/contents/staphylococcal-scalded-skin-syndrome. Accessed June 2025.
11. Society PCD. Epidermolysis bullosa acquisita. Primary Care Dermatology Society. 2021. Available at: https://www.pcds.org.uk/clinical-guidance/epidermolysis-bullosa-acquisita. Accessed June 2025.
12. Society PCD. Mastocytosis. Primary Care Dermatology Society. 2021. Available at: www.pcds.org.uk/clinical-guidance/mastocytosis. Accessed June 2025.
13. DermNet. Congenital erythropoietic porphyria. 2019. Available at: https://dermnetnz.org/topics/congenital-erythropoietic-porphyria. Accessed June 2025.
14. DEBRA: Debra UK. Epidermolysis bullosa (EB): symptoms, treatment, and care. Available at: www.debra.org.uk/get-support/eb-support-and-resources/epidermolysis-bullosa-eb/. Accessed June 2025.
15. Fine JD. *JAMA dermatology*. 2016;152(11):1231–1238.
16. Petrof G, *et al. British Journal of Dermatology*. 2022;186(5):843–848.
17. UpToDate. Epidermolysis bullosa: Epidemiology, pathogenesis, classification, and clinical features. 2024. Available at: www.uptodate.com/contents/epidermolysis-bullosa-epidemiology-pathogenesis-classification-and-clinical-features. Accessed June 2025.
18. Society PCD. Epidermolysis bullosa. Primary Care Dermatology Society. 2021. Available at: https://www.pcds.org.uk/clinical-guidance/epidermolysis-bullosa1. Accessed June 2025.
19. Has C, *et al. BJD*. 2020;183(4):614-627. DOI: 10.1111/bjd.18921.
20. DEBRA International. EB information & resources. 2023. Available at: https://www.debra-international.org/eb-information-and-resources. Accessed July 2025.
21. Brun J *et al. Orphanet Journal of Rare Diseases*. 2017;12(1):119.
22. Kyu-Yeun K *et al. Yonsei Med J*. 2014;55(1):264–269.
23. GOSH Hospital site. Junctional epidermolysis bullosa (EB) severe. 2020. Available at: https://www.gosh.nhs.uk/medical-information-0/generalised-severe-junctional-epidermolysis-bullosa-eb/. Accessed June 2025.
24. UpToDate: UpToDate. Overview of the management for epidermolysis bullosa. Available at: www.uptodate.com/contents/overview-of-the-management-of-epidermolysis-bullosa. Accessed June 2025.