



What is Junctional Epidermolysis Bullosa (JEB) and how is it inherited?

Junctional epidermolysis bullosa (JEB) is an inherited skin disease caused by abnormalities in proteins that hold layers of the skin together¹. Symptoms associated with JEB are attributed to defects in the growth, movement, and attachment of skin cells.

What are the symptoms of Junctional Epidermolysis Bullosa (JEB) and what treatment is available?

JEB is characterized by fragility of the skin and mucous membranes leading to blistering. The more severe form of the disease, Herlitz JEB, includes extensive blistering, recurrent infections, and early death.² Most children with Herlitz JEB do not survive beyond the first year of life due to respiratory complications and infections due to blistering. The non-Herlitz form of the disease is characterized by a reduced tendency to blistering and in most cases is compatible with a normal life span, although there is a life-long tendency to blistering.² Although the types differ in their severity, there is overlap in symptoms.

Symptoms of JEB include³:

- Fragility of the skin and mucous membranes resulting in painful blistering even when there has been little or no trauma. Blistering can be very severe and life threatening, or can be milder and heal without scarring.
- Internal blistering of the throat, esophagus, and upper airway, which can result in obstruction of the airway. Internal blistering is also possible in the stomach, intestines and urinary tract.
- Abnormalities of the urinary tract and bladder, which are present at birth.
- Joint contractures (tightening of the muscles of tendons) caused by lack of motion due to scarring.
- Localized absence of the skin.
- Nail dystrophy (changes in the size, shape, and color of the nails).
- Alopecia (due to loss of hair follicles in areas of scarring).
- Hypotrichosis (lack of hair growth).
- Scarring from blisters that cause fusing of the fingers and toes.
- Risk for development of skin cancer later in life.⁴

There is no cure for JEB. Management involves draining the blisters and protecting the skin with dressings, as well as preventing infection with antibiotics and antiseptics. Attention to fluid balance in infants who are severely affected and consideration of cesarean section to reduce trauma during delivery may be appropriate.³

How is Junctional Epidermolysis Bullosa inherited?

JEB is an autosomal recessive disease that is caused by mutations in four different genes, COL17A1, LAMB3, LAMA3 and LAMC2. Integrate Genetics' Inheritest tests for mutations in three of these genes, LAMB3, LAMA3 and LAMC2, which account for the majority (~88%) of cases of JEB. JEB type and severity of disease cannot be predicted based on an individual's gene mutations.¹

An individual who has only one mutation in any of these genes is a "carrier" and is not expected to have related health problems. An individual who inherits two mutations in the same gene, one from each parent, is expected to be affected with JEB. For example, a child with two *LAMB3* mutations would have JEB, but a child with one *LAMB3* mutation and one *LAMC2* mutation would be only a carrier.

If both members of a couple are carriers of a mutation in the same gene, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.





CARRIER SCREEN

Who is at risk for JEB?

Junctional epidermolysis bullosa can occur in individuals of all races and ethnicities. In the United States, the overall incidence of JEB is approximately 1 in 490,000.⁵

Carrier Frequency in Select Ethnic Groups

Ethnicity	Gene	Carrier Rate
General	LAMB3	1/418 ⁵
Italian	LAMB3	<1/375 ^{2,6}
Italian	LAMC2	<1/425 ^{2,6}

In the Pakistani population a common mutation in the LAMA3 gene has been identified in individuals with the Herlitz form of JEB; however the carrier frequency has not been studied in this population.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

- National Organization for Rare Disorders (NORD): www.rarediseases.org
- EB action network: www.ebanusa.org; (813) 325-1955
- Epidermolysis Bullosa Medical Research Foundation (EBMRF): www.ebkids.org
- Cincinnati Children’s Hospital EB Center: www.cincinnatichildrens.org/eb-center

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