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Junctional epidermolysis bullosa

What is junctional epidermolysis bullosa?

Junctional epidermolysis bullosa is an inherited skin disease caused by abnormalities in proteins that hold layers of the skin together.[1] Symptoms associated with junctional epidermolysis bullosa are attributed to defects in the growth, movement, and attachment of skin cells.

What are the symptoms of junctional epidermolysis bullosa and what treatment is available?

Junctional epidermolysis bullosa is characterized by fragility of the skin and mucous membranes that leads to blistering. The more severe form of the disease, Herlitz junctional epidermolysis bullosa, includes extensive blistering, recurrent infections, and early death. Most children with Herlitz junctional epidermolysis bullosa 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 lifelong tendency to blistering.[2] Although the types differ in their severity, there is overlap in symptoms.

Symptoms of junctional epidermolysis bullosa include:[3]

- Fragility of the skin and mucous membranes that results 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 that are present at birth.
- Joint contractures (tightening of the muscles or 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 junctional epidermolysis bullosa. 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?

Junctional epidermolysis bullosa is an autosomal recessive disease that is caused by mutations in four different genes, *COL17A1*, *LAMB3*, *LAMA3* and *LAMC2*. Three of these genes, *LAMB3*, *LAMA3,* and *LAMC2*, account for the majority of cases of junctional epidermolysis bullosa (~88%). The junctional epidermolysis bullosa type and the severity of disease cannot be predicted based on an individual's gene mutations.[1]

An individual who has 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 junctional epidermolysis bullosa. For example, a child with two *LAMB3* mutations is expected to be affected with junctional epidermolysis bullosa, and a child with one *LAMB3* mutation and one *LAMC2* mutation is 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.

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Who is at risk for junctional epidermolysis bullosa?

Junctional epidermolysis bullosa can occur in individuals of all races and ethnicities. In the United States, the overall incidence is approximately 1 in 490,000.[5] The carrier frequency for *LAMB3*-related junctional epidermolysis bullosa is calculated to be approximately 1 in 418.[5] In the Italian population, the carrier frequency for *LAMC2*-related junctional epidermolysis bullosa is calculated to be approximately 1 in 425.[2,6]

A common mutation in the *LAMA3* gene has been identified in some individuals of Pakistani ancestry with the Herlitz form of junctional epidermolysis bullosa;[7] the carrier frequency has not been calculated for this population.

Having a relative who is a carrier or who is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

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?

Epidermolysis Bullosa Medical Research Foundation (EBMRF): www.ebkids.org

Epidermolysis Bullosa (EB) Center at Cincinnati Children's Hospital: www.cincinnatichildrens.org/eb-center

References

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