

What is xeroderma pigmentosum?

Xeroderma pigmentosum is an inherited disease characterized by extreme sensitivity to sunlight, increased susceptibility to skin and other cancers and, in some cases, neurological abnormalities.^{1,2,3} Individuals with xeroderma pigmentosum have defects in at least eight different proteins important for repairing DNA.¹ Symptoms associated with xeroderma pigmentosum are attributed to the inability of cells to correct normally occurring DNA errors and the resulting accumulation of DNA damage.¹

What are the symptoms of xeroderma pigmentosum and what treatment is available?

Xeroderma pigmentosum varies in severity and age at onset. Signs and symptoms of xeroderma pigmentosum are typically seen in infancy or early childhood and may include:^{1,2,3}

- Severe sunburn after brief sun exposure
- Skin changes, including café-au-lait spots, lentiginosis (freckle-like pigmentation), and xeroderma (dry skin) after exposure to sunlight
- High risk of early (before age 10) and multiple occurrences of skin cancer
- Increased risk of other cancers, including brain, lung, and eye cancer
- Eye problems, including sensitivity to the sun and corneal clouding
- Neurological symptoms including:
 - Hearing loss
 - Coordination and movement problems
 - Loss of intellectual function
 - Difficulty swallowing and talking
 - Seizures

There is no cure for xeroderma pigmentosum.² Management includes avoidance of sun and ultraviolet light exposure, frequent skin examinations by a physician, and periodic eye and neurologic evaluations.³ Affected individuals without neurological abnormalities who observe stringent protection measures may expect to have a normal lifespan.² Individuals with progressive neurological abnormalities may have a shortened lifespan.²

How is xeroderma pigmentosum inherited?

Xeroderma pigmentosum is an autosomal recessive disease caused by mutations in at least eight different genes, including *XPA*, *XPC*, and *ERCC5*.^{2,4-6} 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 has two mutations in the same gene, one from each parent, is expected to be affected with xeroderma pigmentosum. For example, a child with two *XPA* mutations is expected to be affected with xeroderma pigmentosum and a child with one *XPA* mutation and one *XPC* mutation is a carrier.

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

Who is at risk for xeroderma pigmentosum?

Xeroderma pigmentosum is a rare condition that can occur in individuals of all races and ethnicities. It is more common in Japanese and Tunisian populations. The carrier frequency of xeroderma pigmentosum, *XPA*-related, is 1 in 113 in the Japanese population.⁷ The carrier frequency of xeroderma pigmentosum, *XPC*-related, is 1 in 50 in the Tunisian population.⁸

Having a relative who is a carrier or who is affected can increase an individual's risk to be 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?

Genetics Home Reference: <http://ghr.nlm.nih.gov/condition/xeroderma-pigmentosum>

National Organization for Rare Disorders (NORD): <http://rarediseases.org/rare-diseases/xeroderma-pigmentosum/>

References

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