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My46 Trait Profile

Xeroderma pigmentosum

Xeroderma Pigmentosum (XP) is a rare genetic condition where affected individuals have extreme sun sensitivity, which results in an increased chance of developing skin cancer. It is caused by mutations in one of several different genes.

Characteristics of Xeroderma pigmentosum

Xeroderma pigmentosum (XP) is a chromosomal breakage syndrome characterized by hypersensitivity to ultraviolet (UV) radiation. Affected individuals are at risk for severe sunburn, premature skin aging, blistering, rash, and pigmentation abnormalities even after a minimal amount of sun exposure. The risk for skin cancer is greatly increased in individuals with XP. Affected individuals may develop multiple skin cancers over their lifetime. Age of onset and severity are variable, although individuals with classic XP typically develop skin cancer before the age of 20. Malignancies and complications of the eye are frequent and can include light sensitivity, irritation, weakening of the skin surrounding the eye, and possibly blindness. In addition to complications involving the skin and eyes, approximately 25-30% of individuals with XP develop neurological abnormalities such as diminished deep tendon reflexes, progressive hearing loss, intellectual disability, small head-size (microcephaly), poor coordination, and movement problems.

Diagnosis/Testing

The diagnosis of XP is typically based on clinical exam findings and can be confirmed by cellular tests that look for abnormalities in DNA repair. The genes associated with XP are involved in nucleotide excision repair, which is the primary mechanism the body has for repairing genetic damage caused by exposure to ultraviolet radiation. About 50% of XP cases are found to have two abnormal copies of either the XPA or XPC genes. Other genes known to be associated with XP include ERCC3, ERCC2, DDB2, ERCC4, ERCC5, ERCC1, and POLH.

Management/Surveillance

Individuals with XP are highly recommended to avoid sun and UV exposure as much as possible. The application of sunscreen and UV protective clothing is strongly encouraged. Regular skin, eye, and neurological examinations are suggested for individuals affected with XP. Additionally, since management involves limiting sun exposure, there is risk for vitamin D deficiency. Thus, dietary supplementation of vitamin D is often necessary.

Mode of inheritance

XP is inherited in an autosomal recessive pattern. This means that an individual has to inherit two mutations in a gene associated with XP (i.e., one from each parent) to be affected with XP. If both parents are carriers of an XP gene mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with XP.

Risk to family members

Parents of a child with XP are carriers of XP. If a sibling of a child with XP is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of XP.

Special considerations

None

Resources

Xeroderma Pigmentosum Society
http://www.xps.org/
Genetics Home Reference: Xeroderma Pigmentosum
http://ghr.nlm.nih.gov/condition/xeroderma-pigmentosum
XP Family Support Group
http://www.xpfamilysupport.org/

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