Xeroderma Pigmentosum [1]

What is xeroderma pigmentosum?

Xeroderma pigmentosum (XP) is a hereditary condition characterized by extreme sun sensitivity, leading to a very high risk of skin cancer. Eye problems are also common. Neurologic problems—including learning disabilities, progressive hearing loss, progressive neuromuscular degeneration, loss of some reflexes, and occasionally, tumors in the central nervous system—occur in some people with XP.

People with XP are extremely sensitive to ultra-violet (UV) radiation. This includes UVA and UVB. Exposure to even a very small amount of UV radiation leads to severe sunburn and blistering, beginning at a very young age. The sensitivity to UV radiation results in increased freckling, as well as areas of lighter (hypo) skin pigmentation. They also have very dry skin. There is a high risk of squamous cell and basal cell skin cancers [2] and melanoma [3].

People with XP also have eye problems, especially with the eyelids. Like their skin, their eyes are also very sensitive to light, which gives them a slightly increased risk of cancer of the eye [4]. Cancers of the lips, mouth, and the tip of the tongue [5] have also been reported. In addition, people with XP may have neurological complications, including developmental disabilities, mental handicap, and high-frequency hearing loss that leads to deafness.

What causes XP?

XP is a genetic condition. This means that the risk of XP can be passed from generation to generation in a family. Mutations (alterations) in at least eight different genes are known to play a role in XP. Research is ongoing to learn more about XP.

How is XP inherited?

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. XP follows an autosomal recessive inheritance pattern, in which case a mutation must be present in both copies of the gene in order for a person to be affected. This means that both parents must pass on a gene mutation for a child to be affected. A person who has only one copy of the gene mutation is called a carrier. When both parents are carriers of a recessive mutation in the same gene, there is a 25% chance that a child will inherit two mutations and be affected.

Options exist for couples interested in having a child when they know that one of them carries a gene mutation that increases the risk for this hereditary cancer syndrome. Preimplantation genetic diagnosis (PGD) is a medical procedure done in conjunction with in-vitro fertilization (IVF). It allows people who carry a specific known genetic mutation to have children who do not carry the mutation. A woman's eggs are removed and fertilized in a laboratory. When the embryos reach a certain size, one cell is removed and is tested for the hereditary condition in question. The parents can then choose to transfer embryos that do not have the mutation. PGD has been in use for over a decade, and more recently has been used for several hereditary cancer predisposition syndromes. However, this is a complex procedure with financial, physical, and emotional factors for couples to consider before starting. For more information, talk with an assisted reproduction specialist at a fertility clinic.

How common is XP?

XP is considered to be very rare. It is estimated that one in one million people in the United States may have XP. XP appears to be somewhat more common in Japan, North Africa, and the Middle East.

How is XP diagnosed?

XP is suspected when a person shows signs of extreme sun sensitivity. Signs of sun sensitivity include severe burning and blistering with only a small amount of sun exposure or even exposure to fluorescent lights. These signs can be present in infancy. Young children may also be suspected of having XP if they have a large number of freckles on their face. The characteristic eye and neurologic problems may also increase the doctor's suspicion that a person has XP. The clinical signs of XP vary widely, depending on the type of mutations involved and the extent of sun exposure that a person with XP has had.

Genetic testing for mutations in the genes associated with XP is available, mainly as part of research studies. Because there are at least eight genes associated with XP, laboratory screening tests are recommended to help determine which of the eight genes is likely to be causing XP in a family.

What are the estimated cancer risks associated with XP?

People with XP have a nearly 100% risk of developing multiple skin cancers if their environment is not carefully controlled. The first diagnosis of skin cancer commonly occurs in childhood. There may be an increased risk of cancer developing in the eyes and around the mouth area.

What are the screening options for XP?

Current suggested screenings for people who are known or suspected to have XP include:

- Careful skin examination by a doctor every three to six months
- Frequent skin examination by a family member who is familiar with the features of XP-associated skin cancer
- Regular eye examinations by an ophthalmologist, which is a doctor who specializes in the treatment and function of the eye
- Routine neurologic evaluation

Due to the high risk of multiple skin cancers, people with XP should avoid being in the sunlight unprotected, covering the skin completely, and wearing UV-absorbing sunglasses when outside. People with XP are also sensitive to UVC rays given off by some artificial light sources. Halogen bulbs and some fluorescent bulbs emit sufficient UV to burn some individuals, so UV protection indoors may also be needed. Learn more about protecting your skin from the sun [6].

Screening recommendations may change over time as new technologies are developed and more is learned about XP. It is important to talk with your doctor about appropriate screening tests.

Learn more about what to expect when having common tests, procedures, and scans [7].

Questions to ask the doctor

If you are concerned about your risk of skin cancer, talk with your doctor. Consider asking the following questions:

- What is my risk of skin cancer?
- What is my risk of eye cancer?
- What can I do to reduce my risk of cancer?
- What are my options for cancer screening?

If you are concerned about your family history and think you or other family members may have XP, consider asking the following questions:

- Does my family history increase my risk of skin cancer?
- Does it suggest the need for a cancer risk assessment?
- Will you refer me to a genetic counselor or other genetics specialist?

- Should I consider genetic testing [8]?

More Information

The Genetics of Cancer [9]

Genetic Testing [8]

What to Expect When You Meet With a Genetic Counselor [10]

Collecting Your Family Cancer History [11]

Sharing Genetic Test Results with Your Family [12]

Additional Resources

Understanding XP booklet from the National Institutes of Health (PDF)
http://clinicalcenter.nih.gov/ccc/patient_education/pepubs/xp7_17.pdf [13]

Xeroderma Pigmentosum Society
www.xps.org [14]

National Cancer Institute
www.cancer.gov [15]

American Cancer Society
www.cancer.org [16]

Cancer*Care*
www.cancercare.org [17]

To find a genetic counselor in your area, ask your doctor or visit these websites:

National Society of Genetic Counselors
www.nsgc.org [18]

National Cancer Institute: Cancer Genetics Services Directory
www.cancer.gov/cancertopics/genetics/directory [19]

Links
[1] http://www.cancer.net/cancer-types/xeroderma-pigmentosum
[2] http://www.cancer.net/node/31378
[3] http://www.cancer.net/node/31265
[4] http://www.cancer.net/node/31308
[5] http://www.cancer.net/node/31390

[6] http://www.cancer.net/node/24659
[7] http://www.cancer.net/node/24959
[8] http://www.cancer.net/node/24895
[9] http://www.cancer.net/node/24897
[10] http://www.cancer.net/node/24907
[11] http://www.cancer.net/node/30761
[12] http://www.cancer.net/node/24906
[13] http://clinicalcenter.nih.gov/ccc/patient_education/pepubs/xp7_17.pdf
[14] http://www.xps.org/
[15] http://www.cancer.gov/
[16] http://www.cancer.org/
[17] http://www.cancercare.org/
[18] http://www.nsgc.org/
[19] http://www.cancer.gov/cancertopics/genetics/directory