



Understanding Xeroderma Pigmentosum

What is xeroderma pigmentosum (XP)?

Xeroderma pigmentosum (pronounced: zer-o-der-ma/pig-men-toe-sum), XP, is a very rare inherited disease that causes extreme sensitivity to the sun's ultraviolet rays. Unless patients with XP are protected from sunlight, their skin and eyes may be severely damaged. This damage may lead to cancers of the skin and eye. XP has been identified in people of every ethnic group all over the world.

What are the signs of XP?

Many persons with XP will get an unusually severe sunburn after a short sun exposure. The sunburn will last much longer than expected, perhaps for several weeks. This type of sunburn will usually occur during a child's first sun exposure, and it may be a clue to the diagnosis of XP. However, some people with XP will not get a sunburn more easily than others, and the disease will be undetected until unusual skin changes appear over time.

Most patients with XP will develop many freckles at an early age. Continued sun exposure will lead to further changes in the skin, including irregular dark spots, thin skin, excessive dryness, rough-surfaced growths (solar keratoses), and skin cancers. These skin changes will resemble those of elderly people who have spent many years in the sun. In people with XP, these changes caused by sun damage often begin in infancy, and almost always before age 20.

The eyes of a person with XP are often painfully sensitive to the sun and may easily become irritated, bloodshot, and clouded. Noncancerous and cancerous growths on the eyes may occur.

Skin cancers

A series of skin changes leads to the formation of skin cancers. The first skin cancer may develop before a person is 10 years old, and many other skin cancers may continue to form in the future. Cancers develop most often on the face and other sun-exposed parts of the body including the eyes, lips, and tip of the tongue.

All three common types of skin cancer (basal cell carcinoma, squamous cell carcinoma, and melanoma) occur much more often in people with XP. Basal cell and squamous cell carcinomas usually do not spread to internal organs, but they do destroy the local skin and underlying tissues. Melanoma can be fatal if it is not removed before it has spread to internal organs.

Other medical problems

In addition to skin and eye changes, about 20 percent of XP patients may have one or more nerve-related problems including the following: deafness, poor coordination, spastic muscles, or developmental delay. A few people with XP will have all of these problems, and some also may be very short and may not develop normal sexual characteristics.

Some people with XP will develop only mild neurological symptoms in late childhood or adolescence. Whenever neurological problems do occur, however, they usually tend to worsen over time.

What causes XP?

Two factors combine to cause the abnormalities in XP. First, a person inherits traits from each parent which, when combined, lead to an unusual sensitivity to the damaging effects of ultraviolet light. Second, exposure to the sun, which contains ultraviolet light, leads to changes in the skin and eyes.

Problems with DNA damage and repair

Ultraviolet light damages the DNA in cells and disrupts normal cell functioning. DNA (deoxyribonucleic acid) within our genes contains all the coded information needed to direct cell functions.

Damaged DNA is mended by the DNA repair system. But the DNA repair systems of people with XP do not function properly. As a result, unrepaired DNA damage builds up and causes cancerous cell changes or cell death.

How is XP diagnosed?

XP can usually be diagnosed in the laboratory by measuring the DNA repair defect. This test is performed on skin or blood obtained from the patient. Soon, only a few cells may be needed to make this diagnosis.

Different types of XP

There are eight genetic types of XP. Each type is characterized by a different genetic change in the DNA repair system.

Seven of the eight types show reduced activity in one DNA repair system.

The eighth form shows reduced activity in another DNA repair system.

This last type of XP is referred to as the “variant” form, while the other seven types are known as groups A, B, C, D, E, F, and G.

Can XP be treated?

There is no cure for XP, but much can be done to prevent and treat some of the problems it causes:

- protection from ultraviolet light
- frequent skin and eye examinations
- prompt removal of cancerous tissue
- neurological examination
- psychosocial care.

Problems from ultraviolet light

As soon as the diagnosis of XP is suspected, a patient should be completely protected from ultraviolet rays. This will greatly reduce the frequency and severity of skin and eye problems (including cancers).

There are two types of ultraviolet light: short wavelength and long wavelength. The main source of harmful, short wavelength ultraviolet light is sunlight. These ultraviolet rays are also found in the light given off by germicidal lamps, artificial sunlamps (including those found in tanning booths), and mercury vapor lamps. Ultraviolet-measuring instruments, if available, may be used to detect sources of ultraviolet radiation.

The small amount of long wavelength ultraviolet light from sunlight that has

passed through window glass (or produced by unfiltered daylight fluorescent bulbs) is of less risk but probably should be avoided. Regular incandescent light bulbs do not give off ultraviolet light.

To limit a person's exposure to harmful ultraviolet rays, outdoor activity should be restricted to nighttime.

Damaging ultraviolet radiation from sunlight is most intense at midday. In some patients, even a few minutes of sun exposure at midday may cause a severe sunburn. If daytime exposure is unavoidable, it should be limited to the very early morning or very late afternoon hours—a time of day when your shadow is much longer than your height.

When XP patients are indoors or in a car, the windows should always be closed because glass blocks harmful ultraviolet rays from sunlight.

Tips for protecting children

- Children with XP should not play outdoors during the day unless they are under ultraviolet light-blocking shelters and away from reflective surfaces such as snow, sand, or water. Clouds do not block out harmful rays.
- Special arrangements for children with XP should be made at school to ensure that they are not exposed to sunlight from an open window, that they are not exposed to any unfiltered (bare) fluorescent light bulbs, and that they are not permitted outside for gym, recess, fire drills, or other activities.



A well-protected person with XP.

Daily protection outdoors

- When patients with XP are outdoors in daylight, they should wear long sleeves, long pants, and wide-brimmed hats. Two layers of clothing protect more than one layer. Tightly woven fabrics generally give more sun protection than loose weaves.
Wear clothing that you can't see the light through. Some companies make light-weight clothing specifically designed to provide a high degree of sun protection.
- Choose eyeglasses or sunglasses specifically labeled to block ultraviolet light completely. Glasses with side-shields protect the eyelids and skin around the eyes. Long hair styles help protect the neck and ears.

- While sun protection by clothing is most effective, any skin not covered by clothing or hair should be protected by sunblocks such as zinc oxide, titanium dioxide, sun-blocking makeup, or sunscreens. Sunscreens with a sun protection factor of 15 or higher should be used. They should be applied at least 30 minutes before going out in the sun. Lip moisturizers containing sun blocking agents also give protection.
- A sunscreen may also be used indoors to protect against unrecognized sources of ultraviolet light.

What else can cause harm besides ultraviolet light?

Laboratory tests indicate that sunlight is the major DNA damaging agent to the cells of XP patients. However, tobacco smoke and some drugs (such as psoralens, used with ultraviolet light for treating psoriasis) can cause similar DNA damage. People with XP should avoid exposure to tobacco smoke and should not use tobacco products because they are probably at greater risk for developing lung cancer.

What more can I do?

Frequent skin examinations

Patients should be examined often by a family member or another person who has been taught to recognize the signs of skin cancer. Any suspicious spot or growth should be immediately reported to the patient's doctor. Examinations should include the eyes, scalp, ears, mouth, tongue, nostrils, and all other areas of the skin, even those that do not have sun exposure (for example, the buttocks).

Examination by a dermatologist (a doctor specializing in skin disorders) should take place at least every 3 to 6 months. The dermatologist can help detect skin cancers before they have grown or spread to internal organs. A small piece of suspicious skin growths may be removed (biopsied) and examined for cancer.

Prompt removal of cancerous tissue

Skin cancer treatment for XP patients is similar to that for anyone with skin cancer. Treatment may include removal of the cancer by freezing, use of an electric needle, or surgery. Depending on the size, type, and location of the cancer, a small cancerous growth can usually be treated in a doctor's office. Large tumors may require extensive surgery and skin grafting. Dermabrasion or removing large portions of skin with grafting has been used for some patients with extensive involvement. X-ray treatment has also been used safely. Precancerous growths, such as solar keratoses, may be frozen with liquid nitrogen.

Other skin treatments

Some patients with XP who have had many skin cancers have prevented new cancers by taking a drug called isotretinoin, a derivative of vitamin A. However, this medicine has serious side effects that prevent its use in all but the most severe cases.

A cream containing a DNA repair enzyme is currently being studied.

Frequent eye examinations

Examination by an ophthalmologist (a doctor specializing in the eye) should take place regularly. The ophthalmologist can help detect eye cancers and other lesions before they become a problem.

Artificial tears may soothe abnormally dry or irritated eyes. If the corneas of the eyes become so clouded that the patient cannot see, a corneal transplant may be considered to restore vision.

Treatment of neurological problems

About 20 percent of patients develop neurological problems. While nothing can prevent or stop these problems from occurring, it is important to be aware of them. Early testing and treatment for potential neurological problems may lessen the unfortunate results of undetected abnormalities.

For example, detection of hearing loss and subsequent use of a hearing aid may lessen difficulties in communication and in school. Patients with XP should have periodic neurological examinations.

The role of sun exposure in the development of neurological problems

Researchers do not believe that sun exposure affects the development of neurological problems in patients with XP. The sun's ultraviolet rays are absorbed by the skin and do not penetrate the brain or other internal organs.

But no matter how small his or her sun exposure, a person with XP who is genetically prone to develop neurological symptoms will do so. While the cause of the neurological problems is unclear, it appears that persons with the most severe

reductions in their DNA repair ability are the most likely to have such problems.

Psychosocial aspects of XP

Persons with XP and their families face many challenges in daily living. This disease has many long-term physical, emotional, social, and economic consequences.

Skin changes, including cancers at an early age and other physical problems, may affect school experiences, employment opportunities, recreational activities, and social relationships.

Coping with chronic illness and disability is very difficult. Some people have problems with health insurance or finances while others may feel anxious or depressed. Persons with XP need a great deal of support from family, friends, and their communities to provide encouragement, build confidence, and give hope. Patients with XP and their families may obtain assistance from their physician, nurse, or social worker.

What is the life span of people with XP?

Many people with XP will die at an early age from skin cancer if they are untreated and unprotected from sunlight. However, if a person is diagnosed early, has no severe neurological problems, is protected from ultraviolet light, and followed carefully for early cancer detection, a normal life span is possible. The life spans of most persons with XP will fall between these extremes. A reduced life span is to be expected, but there are great differences among patients with XP.

What part does heredity play?

XP is a recessive condition. This means that a person must have two XP genes (one from each parent) to develop the disease. Both parents of a person with XP are carriers of the XP trait because each parent has one XP gene and one normal gene. Neither parent has symptoms of XP. Recent advances in understanding XP make it possible to test if someone is a carrier of some forms of XP by analyzing that person's DNA.

If the parents of a child with XP have another child, will that child also have XP?

There is a one in four chance that any child of the same parents of a patient with XP will also have XP. XP among affected children in the same family is usually of similar severity. For example, if the first child with XP has severe neurological problems, the next affected child may have similar problems.

Prenatal diagnosis of XP has been done in research laboratories, but it is not a routine test. Parents of a child with XP should seek genetic counseling before considering having another child.

Can a person with XP have children?

Most people with XP have normal sexual development and functioning, and they are able to have children. The advisability of a person with XP becoming a parent would be affected by the person's own ability to care for a family.

The probability of a person with XP having a child with XP is very small. This would occur only if the other parent also has XP or is a carrier for the XP trait. In some cases, carriers of the XP trait can be detected by a laboratory test of their DNA repair genes.

What research is being done?

Researchers in the United States and throughout the world are learning about XP and trying to correct the DNA repair defect in laboratory-grown cells from patients with XP. The genes causing most types of XP have been identified. Many laboratories in the US, Europe, and Japan are studying XP genes and trying to understand what they do. Clinical studies on skin cancer prevention with oral medications and evaluating patients with unusual features are also being conducted at the National Institutes of Health.

Where can I get more information?

Information for patients and collection of clinical data about symptoms, treatment, and progress of patients with XP is available from the following organization:

Support groups have formed and can be contacted as follows:

United States

Xeroderma Pigmentosum society
437 Snyderstown RD
Crayville N.Y. 12521
(877) XPS-CURE
www.xps.org

Xeroderma Pigmentosum Family
Support Group
8375 Folsom BLVD Suite 201
Sacramento CA, 95826
1-949-218-9401
www.xpfamilysupport.org

Great Britain

XP Support Group
2 Strawberry Close
Prestwood
Great Missenden
Bucks
Hp16056
UK
www.xpsupportgroup.org.uk

Your dermatologist can answer
specific questions about this
disease. Additional information may
be obtained from these sources:

Task Force on Xeroderma
Pigmentosum
American Academy of
Dermatology
Box 4014
Schaumburg, Illinois 60168-4014
(708) 330-0230

National Cancer Institute
Office of Cancer Communications
31 Center Drive MSC 2580
Building 31 Room 10A16
Bethesda, Maryland 20892-2580
(for cancer information)

1-800-422-6237 (9 a.m. to
4:30 p.m.)

**Local Branches of the American
Cancer Society**

(for cancer information)



2006

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