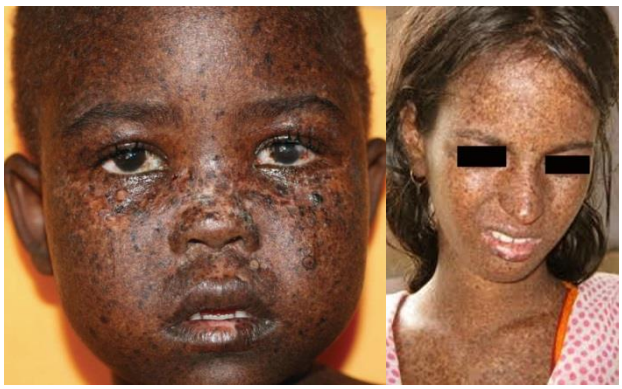
Cancer Association of South Africa (CANSA)

Fact Sheet
on
Xeroderma Pigmentosum

Introduction

Xeroderma pigmentosum, or XP, is an autosomal recessive genetic disorder of DNA repair in which the ability to repair damage caused by ultraviolet (UV) light is deficient. In extreme cases, all exposure to sunlight must be forbidden, no matter how small; as such, individuals with the disease are often colloquially referred to as *Children of the Night*.



[Picture Credit: XP]

Multiple basal cell carcinomas (basaliomas) and other skin malignancies frequently occur at a young age in those with XP. In fact, metastatic malignant melanoma and squamous cell carcinoma are the two most common causes of death in individuals with XP. This disease involves both sexes and all races.

Xeroderma Pigmentosum (XP)

Xeroderma pigmentosum, which is commonly known as XP, is an inherited condition characterised by an extreme sensitivity to ultraviolet (UV) rays from sunlight. This condition mostly affects the eyes and areas of skin exposed to the sun. Some affected individuals also have problems involving the nervous system.

The signs of XP usually appear in infancy or early childhood. Many affected children develop a severe sunburn after spending just a few minutes in the sun. The sunburn causes redness and blistering that can last for weeks. Other affected children do not get sunburned with minimal sun exposure, but instead tan normally.

By age 2, almost all children with XP develop freckling of the skin in sun-exposed areas (such as the face, arms, and lips); this type of freckling rarely occurs in young children without the disorder. In affected individuals, exposure to sunlight often causes dry skin (xeroderma) and changes in skin colouring (pigmentation). This combination of features gives the condition its name, Xeroderma Pigmentosum.

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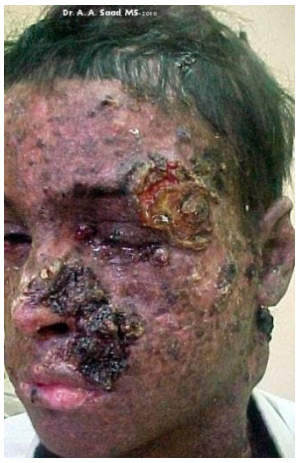
People with XP have a greatly increased risk of developing skin cancer. Without sun protection, about half of children with this condition develop their first skin cancer by age 10. Most people with XP develop multiple skin cancers during their lifetime. These cancers occur most often on the face, lips, and eyelids. Cancer can also develop on the scalp, in the eyes, and on the tip of the tongue.

Studies suggest that people with XP may also have an increased risk of other types of cancer, including brain tumours. Additionally, affected individuals who smoke cigarettes have a significantly increased risk of lung cancer.

The eyes of people with XP may be painfully sensitive to UV rays from the sun. If the eyes are not protected from the sun, they may become bloodshot and irritated, and the clear front covering of the eyes (the cornea) may become cloudy. In some people, the eyelashes fall out and the eyelids may be thin and turn abnormally inward or outward. In addition to an increased risk of eye cancer, XP is associated with noncancerous growths on the eye. Many of these eye abnormalities can impair vision.



[Picture Credit: Stage III XP]

About 30 percent of people with XP develop progressive neurological abnormalities in addition to problems involving the skin and eyes. These abnormalities can include hearing loss, poor coordination, difficulty walking, movement problems, loss of intellectual function, difficulty swallowing and talking, and seizures. When these neurological problems occur, they tend to worsen with time.

Researchers have identified at least eight inherited forms of XP: complementation group A (XP-A) through complementation group G (XP-G) plus a variant type (XP-V). The types are distinguished by their genetic cause. All of the types increase skin cancer risk, although some are more likely than others to be associated with neurological abnormalities.

Lucero, R. & Horowitz, D. 2020.
"Xeroderma pigmentosum (XP) is a rare autosomal recessive genodermatosis that results due to mutations in nucleotide excision repair. The condition characteristically demonstrates severe photosensitivity, skin pigmentary changes, malignant tumor development, and occasionally progressive neurologic degeneration. The disease affects about 1 per million in the United States, and the incidence in Japan is much higher at 45 per million.
Dermatologist Moriz Kaposi first described xeroderma pigmentosum in 1874. Dr. Kaposi described patients with dry skin, pigmentary changes, and the development of multiple skin tumors at a young age. Further studies over the next several decades highlighted the importance of severe photosensitivity in the pathophysiology of xeroderma pigmentosum. In the 1960s, Dr. James Cleaver performed studies on cultured fibroblasts from patients with xeroderma pigmentosum and found the fibroblasts to have defective DNA repair after UV exposure. Further studies showed that xeroderma pigmentosum patients with neurologic manifestations have even less effective DNA repair after UV exposure compared to patients with XP without neurologic manifestations. These studies have enhanced knowledge about the connections between UV exposure, DNA damage and repair, and the development of malignant tumors."

Incidence of Xeroderma Pigmentosum in South Africa
The National Cancer Registry (2017) does not provide any information regarding the incidence of Xeroderma Pigmentosum in South Africa.

Causes of Xeroderma Pigmentosum (XP)
Xeroderma pigmentosum is an autosomally recessive inherited disease, which means that one must inherit two recessive XP genes (one from each parent). If one's parents are only carriers of the XP trait (each have one XP gene and one normal gene), they will not show signs or symptoms of the disease. By having the two XP genes this causes one to have an extreme sensitivity to UV light and as a result experience a range of signs and symptoms of XP. At least eight different gene abnormalities or complementation groups have been described in different families (XPA to XPG) resulting in varying disease severity.

Essentially, the signs and symptoms of XP are a result of an impaired DNA repair system. In people who do not have XP, cell damage from UV light is mended by the DNA repair system. However, people with XP have a defect in this repair system and any damaged cells from UV light remain unrepaired, leading to cancerous cells or cell death.

Symptoms of Xeroderma Pigmentosum (XP)
The following symptoms may appear:

- Sunburn that does not heal after just a little bit of sun exposure
- Blistering after just a little bit of sun exposure
- Spider-like blood vessels under the skin
- Patches of discoloured skin that get worse
- Crusting of the skin
- Scaling of the skin
- Oozing raw skin surface
- Discomfort when being in bright light (photophobia)
- Skin cancer

Differential Diagnosis
There are other causes of photosensitivity, e.g., congenital erythropoietic porphyria.

Other genetic conditions with photosensitivity due to defective DNA repair - eg, Cockayne's syndrome, the XP-CS complex, trichothiodystrophy (TTD), the XP-TTD complex, cerebro-oculo-facio-skeletal (COFS) syndrome and the UV-sensitive syndrome.
(Patient Info).

Treatment of Xeroderma Pigmentosum (XP)

Children with this condition need total protection from sunlight - even the light coming through windows or from fluorescent bulbs is dangerous.

[Picture Credit: Xeroderma Pigmentosum Boy]

When these children go out in the sun, they need to wear special protective clothing.

Use high SPF protection sunscreen and very dark, UV sunglasses. The doctor may prescribe medicine to help prevent certain precancerous growths from becoming skin cancers.
Many patients with Xeroderma Pigmentosum may die at an early age from skin cancers. However, if a person is diagnosed early, does not have severe neurological symptoms or has a mild variant, and takes all the precautionary measures to avoid exposure to UV light, they may survive beyond middle age.

Patients with Xeroderma Pigmentosum and their families may face many challenges in daily living. Constant educating and reminding of the need to protect oneself from sunlight is paramount to the management of Xeroderma Pigmentosum.

Lehmann, A.R. & Fassihi, H. 2020.
"Xeroderma pigmentosum (XP) is a well-studied disorder of (in most cases) nucleotide excision repair. The establishment in 2010 of a multidisciplinary XP clinic in the UK has enabled us to make a detailed analysis of genotype-phenotype relationships in XP patients and in several instances to make confident prognostic predictions. Splicing mutations in XPA and XPD and a specific amino acid change in XPD are associated with mild phenotypes, and individuals assigned to the XP-F group appear to have reduced pigmentation changes and a lower susceptibility to skin cancer than XPs in other groups. In an XP-C patient with advanced metastatic cancer arising from an angiosarcoma, molecular analysis of the tumour DNA suggested that immunotherapy, not normally recommended for angiosarcomas, might in this case be successful, and indeed the patient showed a dramatic recovery following immunotherapy treatment. These studies show that molecular analyses can improve the management, prognoses and therapy for individuals with XP."

Genetic Counselling and Risk to Relatives

Inheritance of Xeroderma Pigementosum (XP) is autosomal recessive. If parents are considering further pregnancies, prenatal diagnosis is often possible. Where XP is suspected, siblings should be protected from UV light until XP can be excluded.

Recent investigations of heterozygotes with one of four XP genes (XPA, XPC, ERCC2, or ERCC5) have reported an increased risk of skin cancer, lung cancer, or altered response to certain chemotherapeutic agents.

The South African Xeroderma Pigmentosum Society Contact Details

The XERODERMA PIGMENTOSUM SOCIETY is a Non Profit Company incorporated in South Africa on January 13, 2010. Their business is recorded as In Business. The activity is registered as NON PROFIT SUPPORT GROUP TO RELIEVE THE NEEDS OF PERSONS WITH XERODERMA PIGMENTOSUM (XP) AND RELATED CONDITIONS AS WELL AS FAMILY SUPPORT. It is not part of a group. The company was incorporated 6 years ago.

Xeroderma Pigmentosum Society

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Sources and References Consulted or Utilised

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http://www.dermnetnz.org/systemic/xeroderma-pigmentosum.html

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Patient Info
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Stage III XP
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XP
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