

REVIEW ARTICLE

Living with xeroderma pigmentosum: comprehensive photoprotection for highly photosensitive patients

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SUMMARY

Xeroderma pigmentosum (XP) is a rare autosomal recessive disease of deoxyribonucleic acid (DNA) repair with ultraviolet (UV) radiation sensitivity and a 10 000-fold increased risk of skin cancer. Symptoms include: freckle-like pigmentation in sun-exposed skin before age 2 years, severe burns after minimal sun exposure (50% of patients) and damage to exposed surfaces of the eyes with loss of vision and ocular cancer. About 25% of patients develop a progressive neurodegeneration. The combination of an inherited inability to repair UV-induced DNA damage and environmental exposure to UV must occur for cutaneous and ocular symptoms to develop. There is no cure for XP, but many of its manifestations may be reduced or prevented through consistent UV protection; thus XP serves as a model for sun protection of patients with marked photosensitivity. Sun protective clothing including hats, sunglasses and face shields, sun screen lotions and avoidance of environmental sources of UV are cornerstones of prevention of skin and eye damage and cancer. Although XP is a serious disease with the potential for limitation of life expectancy, XP patients can live active lives while at the same time avoiding UV.

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Xeroderma pigmentosum (XP) can serve as a model disease for protection of patients with marked photosensitivity. XP is a rare autosomal recessive disease of deoxyribonucleic acid (DNA) repair characterized by severe ultraviolet (UV) sensitivity resulting in a 10 000-fold increased risk for cancer in UV-exposed tissues (1). Symptoms include: freckling in sun exposed skin before age 2 years, severe burns after minimal sun exposure (50% of patients), and skin cancers in children and adults with a median age of less than 10 years. UV damage to the eyes can result in loss of vision and ocular cancer. About 25% of patients develop progressive neurodegeneration including sensorineural hearing loss, dysphagia, ataxia, and premature death. XP patients may have mutations in any one of seven genes involved in the nucleotide excision repair pathway: XP-A, XP-B, XP-C, XP-D, XP-E, XP-F, and XP-G. The XP variant type is caused by mutations in an eighth gene, which encodes pol eta, a protein involved in trans-lesion synthesis (2, 3). XP patients with mutations in the XP-A, B, D, F, and G genes experience severe sun burning after minimal exposure, whereas patients with mutations in XP-C, E, and V do not exhibit this exaggerated burning and can even tan, but they do develop pigmentary abnormalities including freckles and lentigos (1, 4–6).

XP is an excellent example of gene/environment interaction. The combination of an inherited inability to repair UV-induced DNA damage plus environmental exposure to UV must occur for cutaneous and ocular symptoms to develop. If XP patients are diagnosed early in life and stringent UV protection is consistently maintained, the amount of DNA damage and subsequent skin cancers and ocular damage may be minimized. However, UV protection does not prevent the neurodegeneration (1, 7, 8).

EFFECTS OF UV ON XP PATIENTS

The cutaneous symptoms of XP start in early childhood and may include, in some patients, sunburns occurring after minimal sun exposure. People with XP have burned after being outside for only a few minutes and some can burn through window glass. These burns can be so severe that parents have been suspected of neglect or abuse. (Fig. 1) Over time, freckle-like, hyperpigmented macules



Fig. 1. Sunburning in XP-D patient and lack of burning in XP-C patients. (a–c) XP-D patient (XP499BE) who sustained severe blistering sunburn following intermittent evening sun exposure. (a) Five months of age: day 8 after sun exposure – swelling and burns of face resolving with delayed erythema on dorsum of right arm and hand. (b) Day 8 after sun exposure – delayed swelling, erythema, blistering, and peeling on dorsum of left hand and wrist. (c) Age 11 months: excellent sun protection and normal skin exam. (d and e) XP-C siblings with no history of burning on minimal sun exposure. (d) Older sister age 12 (XP198BE) – diagnosed at age 1 year secondary to freckling on face, hands, and arms. She had excellent UV protection since diagnosis and had 1 BCC in her scalp; (e) Patient XP338BE, 7-year-old brother of patient XP198BE. He had excellent UV protection since diagnosis at birth and no clinical evidence of XP. (f) XP-C patient (XP24BE) age 32 years, did not have a history of burning on minimal sun exposure. She had a relatively late age of diagnosis (age 8 years) and poor UV protection. She has multiple lentiginos, cheilitis, telangiectasias, and > 200 skin cancers. She died at age 35 years of a glioblastoma of her brain (21).

(lentigines) of irregular size, shape, and color develop in the areas of sun exposure (1, 8–11).

About 50% of XP patients do not sustain blistering burns; they tan and develop lentigines on UV/sun-exposed skin, often before age 2. Indeed, the presence of lentigines on sun-exposed skin before age 2 years is an important feature that may distinguish XP from other sun sensitive disorders. Frequently, there is a marked cut off of freckling between sun exposed and nonsun exposed (protected) skin. Unprotected XP patients develop dry skin (xeroderma) and poikiloderma with the appearance of marked photoaging. They may develop hundreds of skin cancers including melanomas, basal cell, and squamous cell carcinomas, including developing sunlight induced cancers on the lips and tip of the tongue. Lip and tongue tumors can metastasize to cervical lymph nodes and to more distant areas in the head and neck (9, 11, 12).

A study of XP patients evaluated at the National Institutes of Health (NIH) found the median age of first nonmelanoma skin cancer (either basal cell or squamous cell carcinoma) was 9 years, in contrast to 67 years of age in the general population (1). Patients with XP develop melanomas at a 2000-fold increased rate before the age of 20 years. The median age at first melanoma cancer in XP patients in the NIH study was 22 years, which is 33 years younger than that of the general population (1).

Remarkably, XP patients who sustain sunburns may have fewer skin cancers than nonburning patients; this may be because the XP patients who burn are so sensitive that as children they are protected by their parents from sun exposure and may be more diligent with sunscreen use as adults (1).

The anterior surfaces of the eyes (cornea, sclera, eyelids, and surrounding tissues) of XP patients are particularly vulnerable to the damaging effects of UV. The anterior tissues shield the posterior parts of the eye that are spared UV damage (13). After prolonged UV exposure, the corneas can become cloudy, with neovascularization pinguecula and pterygium (6, 12, 14, 15). Chronic UV-induced eye damage and the development of cancers (basal cell, squamous cell carcinomas, and melanomas) on the cornea and surrounding tissues of the eyes including the lids can lead to vision loss (6, 12, 14–16).

In addition to the skin disease, approximately 25% of XP patients develop progressive neuro-degeneration (1, 6, 8, 11, 15, 17–19) that may include sensorineural hearing loss, ataxia, and cognitive decline. The patients who eventually manifest XP neurologic disease are often very sun sensitive and will have the severe blistering sun burns. However, not all XP patients who burn will develop neurologic disease (1, 6–8, 17, 19–21).

UV PROTECTION FOR THE XP PATIENT

By reducing environmental UV exposure, persons with XP can substantially diminish the amount of damage they sustain and, consequently, the number of skin cancers and the extent of other complications (11, 22). The goal of UV protection is to significantly lessen the amount of UV radiation reaching the tissues of XP patients. There is no ‘magic’ formula to know how much UV is tolerable; so many patients aspire to minimize exposure as much as possible. The process of UV protection can be thought of as wrapping the XP patients in layers of protection: an outer layer of environmental UV management, a middle layer of mechanical barriers (clothing), and an innermost layer of protection next to the skin (sunscreen/blocking lotions) (7, 22, 23).

MODIFICATION OF THE ENVIRONMENT

As soon as the diagnosis of XP is considered, the patient should be protected from UV. Sunlight is by far the most significant source of UV. Restricting outdoor activity to either very early in the morning or later in the evening, after the sun is below the horizon, is optimal. XP patients can use UV meters, which can be reasonably priced, that measure the levels of both UVA and UVB in the environment. Ideal meters are easy to carry in a purse or back pack, easy to read, and relatively sturdy. Measuring UV levels outdoors and indoors can identify areas of high UV and provide guidance for limiting exposure. There is no absolutely safe meter reading, however, by maintaining a very low UV environment, exposure can be minimized. UV-blocking film is available for windows in homes and cars to eliminate virtually all incoming UV radiation (7, 22–24). The film does not have to be darkly tinted to block UV, as it is not in the visible spectrum of light.

Interior lighting can also be a source of UV. Although incandescent bulbs tend to emit little to no UV, unshielded florescent bulbs, mercury vapor lamps, and halogen bulbs can be significant sources. Placing plastic sleeves, coverings, or shields over florescent bulbs and replacing halogen bulbs with either incandescent or LED bulbs can significantly reduce the amount of interior UV.

As limiting the amount of outdoor UV exposure is critical, XP patients should have handicapped placards for their cars, so they can park as close as possible to public facilities. School age XP children should be transported to schools in ‘UV safe’ buses or by their parent in a car with UV-blocking filmed windows (22–24). In the United States, students are entitled to a safe environment for their education. The school authorities may have to modify

classrooms to reduce UV exposure for XP students. Establishing an Individualized Educational Plan for the XP child will ensure his or her full participation in school activities as is possible in a UV-safe environment.

PROTECTIVE CLOTHING

UV in the environment is physically blocked from reaching the skin surface by clothing. People with XP should wear long-sleeved shirts and long pants; girls and women can wear dresses and skirts along with tights and leggings to ensure full photoprotection. Ideally, fabric should be dense, darker, and tightly woven. Thus, denim and synthetic fabrics such as polyesters and rayon are good choices. Assessing a fabric for its UV-blocking ability is relatively simple; hold the fabric up to a light source and if visible light passes through the weave, then UV is also passing through. This assessment can also be achieved by holding a UV meter under the fabric while in front of a UV emitting light source. Socks and closed toe shoes can minimize the chance of inadvertently exposing skin around the feet and ankles to UV. When XP patients are in high UV areas, gloves made of UV-blocking material should also be worn to prevent exposure of hands and wrists. In general, layering clothes provides greater UV protection.

Special UV-blocking clothing is commercially available; in addition to its tight weave, this clothing is light weight and treated with UV absorbers and blockers. The UV protection factor (UPF) is frequently used to indicate how much UV can penetrate a fabric. The higher the UPF, the better the clothing blocks UV. One drawback to this specialized clothing is that it can be very expensive, especially for rapidly growing children, and it may not come in smaller sizes. Another option is to wash normal tightly woven clothing with commercially available 'sun blocking' rinses or treat it with UV blocking fabric sprays.

The scalp around the part in hair, the face, and eyes of XP patients are particularly vulnerable to UV damage and subsequent development of skin cancers. XP patients should wear large brimmed sun hats (made from UV-blocking material), and many patients will also have a clear UV-blocking plastic shield attached to the hat that covers the whole face. The hat will often have an attached piece of UV-blocking cloth sewn onto the back to protect the back of the head and neck (Fig. 2). Patients can wear these head coverings (often referred to as their 'hood') when at risk for significant UV exposure. Many patients may be photophobic and wear UVA and UVB blocking sunglasses that provide full eye coverage (including side shields) to keep them more comfortable and provide additional UV protection (16, 22–24).

SUNSCREEN USE

XP patients should use a highly effective sun screen on a daily basis. The first application in the morning should be to all areas of the skin. During the day, sunscreen should be reapplied every 2–3 h to the face, neck, ears, and hands and any area not continually covered by clothing. Sunscreens should be SPF 30 or greater. Commercially available sunscreens come in multiple combinations of ingredients and formulations; it is important for XP patients to use a sunscreen that is both UVA and UVB blocking and in a preparation that is easy to apply, comfortable to wear, and acceptable to the patient for daily use. The cost for sunscreens can vary widely. As XP patients need to wear significant amounts of sunscreen on a daily basis, it is important for them to find one that is reasonably priced and readily available (22–24).

MEDICAL CARE

Vitamin D is formed in the skin following sun exposure and well-protected individuals may be at risk for defi-



Fig. 2. Well-dressed XP patient. XP-D Patient XP341BE, age 4 years, is wearing long sleeves, long pants (denim), UV-blocking gloves, closed toe shoes, and UV blocking 'hood' with clear face shield. He is wearing sunglasses for eye protection as well as for reduction in his photophobia.

Table 1. XP patient support groups

Country/location	XP patient support group	Website
United States	XP Family Support Group	http://www.xpfamilysupport.org
United States	XP Society	http://www.xps.org
North America	XP Grupo Luz De Esperanza (in Spanish)	http://www.xpgrupoluzdeesperanza.org
Great Britain	XP Support Group	xpsupportgroup.org.uk
France	Les Enfants De La Lune	asso.orpha.net/AXP/debut.htm
Germany	Xeroderma pigmentosum	http://www.xerodermapigmentosum.de/
Tunisia	Association d'aide aux Enfants Atteints de Xeroderma Pigmentosum	http://www.xp-tunisie.org.tn
Japan	Japanese National Network of Xeroderma Pigmentosum	http://www.xp-japan.net
Turkey	Xeroderma Xpturkiye	None
South Africa	Xeroderma Society South Africa	Website in construction

ciency. With adequate diet, it is possible for XP patients to have nearly normal levels of vitamin D in their blood (25). However, the well-protected XP patient can become vitamin D deficient if dietary intake of vitamin D is poor. Serum vitamin D levels should be monitored regularly with supplementation with oral vitamin D for low serum levels. On occasion, XP patients have been noted to be osteopenic based on bone density measurements and are at risk for fractures (24).

UV SAFE LIVING

There are several guidelines for living a UV safe lifestyle: reducing the amount of environmental UV exposure, preventing UV from reaching exposed tissues through the use of clothing and sun screens, and adjusting lifestyle choices to conform to low UV requirements. At the time the diagnosis is made, physicians can educate the family/patient about UV protection for their child or themselves. Frequently, they will have limited knowledge as to specific 'hands on – how to do it' information of living with the condition. Over the past several years, XP patient support groups have been formed throughout the world including the United States, Europe, Africa and the Middle East, and Japan (Table 1). Groups provide education about living with XP and social support activities for XP patients and their families. These groups assist families and XP patients through the initial crisis situation and help them establish a 'new normal' for living with XP and UV protection. The support groups are made up of families of XP children and XP adult patients who have adjusted to living with XP. The groups serve as a means of sharing knowledge and experience about living with XP and mutual support can help reinforce patients to adhere to their sun protection program. The support groups have Internet websites,

Facebook pages, and some have free educational pamphlets. They also may provide direct personal contact via telephone and email. They often arrange family gatherings where XP children, adults, and families can meet in a UV-safe environment. These provide a forum for education about living with XP and a program of fun and fellowship. As the incidence of XP is approximately one in a million in the United States and rare throughout the world, these resources help reduce isolation (11, 22, 23, 26, 27).

Support groups may assist families in obtaining UV-blocking window film for their homes and cars, UV meters, and provide instructions and UV blocking flexible plastic for making the UV blocking hoods (Table 1). Some assist in providing sunblock lotions and hearing aids (1, 11, 22, 23).

SOCIAL/FAMILY/COMMUNITY INTERACTIONS

Living UV safe is a significant adjustment (Table 2). Balancing the needs of UV safety for the affected family member with the needs of unaffected members can be daunting. XP families have developed ingenious ways to integrate UV-safe activities into their community. One family has a yearly 'glow in the dark' nighttime Easter egg hunt for their XP child and neighborhood children. Another family had their garage converted into an indoor UV safe playroom with a sandbox, and wading pool, where the XP child and his friends can play. Social and family support is extremely important for XP families especially after the diagnosis is first made; if families are already struggling with issues such as poverty, substance abuse, domestic violence, or mental illness, the ability to provide a UV-safe environment for the XP patient may be compromised. Social service agencies, schools, religious

Table 2. UV safe living

Environmental factors	
UV meters:	Assess ambient levels of environmental UV to assure safe levels
Limitation of outdoor activities:	Remaining indoors or heavily covered outside; when sun is above horizon
Use of low UV lighting	Shield florescent, incandescent or LED bulbs
UV-blocking films for windows:	Apply films to windows in homes, cars, schools, work places. Any indoor areas where XP patients will be spending extended periods of time.
Clothing	
Styles:	Long, pants and long sleeved shirts, tights or leggings; double layers of clothing provide better protection
Fabric types:	Dense dark tightly woven fabrics – denim; polyesters and rayon; Specially manufactured UV blocking clothing
Hats, hoods, sunglasses	Hats wide brimmed made from UV blocking cloth; hoods with clear plastic face shields, UVA and UVB blocking sunglasses
Other clothing	Closed toed shoes, socks, gloves
Sunscreen	
UVA and UVB blocking	Easy to apply, comfortable to wear not expensive and acceptable to the patient for daily use
Lifestyle factors	
Social support	XP support groups, schools, social service agencies, religious agencies
Ongoing environmental assessment	Using UV meters to determine safe areas in new environments such as schools, medical facilities, work places, stores
Living an active life style	Handicapped parking placards, medic alert bracelets, indoor career planning

organizations, and the XP support groups may all get involved to help patients and families in these circumstances (1, 11, 22, 23).

Because environmental management is a significant piece of UV protection, patients and families must constantly be mindful of UV levels in their immediate surroundings. Most XP children and many XP adults have their UV-protective hoods with them at all times. Families and patients will often ‘meter’ a public space to assess the ambient UV levels prior to entering the area unprotected by their hood and clothing (1, 11, 22–24).

Planning for medical appointments and surgical procedures can be very complex and requires XP patients, families, and medical professionals to closely collaborate in the UV assessment of the environment. Assessments for UV levels of lighting in the medical facilities is important before treating the XP patient. As an example, making sure the XP patient is in a bed away from a window or if hospital corridors are lighted with high UV emitting florescent bulbs allowing the XP patient to wear a ‘hood’ while passing through the unsafe areas. In addition, it is important to assess any UV-emitting instruments used during the procedure and determinate if any alternatives are needed or look for ways to shield the patient during the procedure. Some XP families have purchased their own otoscopes that use non-UV-emitting LED bulbs as many

regular otoscopes and other exam lights can contain high UV-emitting halogen bulbs.

Automobile accidents and other emergencies are examples where the XP patient or family may not be able to communicate the need for UV protection. XP patients may wear medical alert jewelry (bracelets or necklaces) or carry medical alert cards in their purses or wallets, so that first responders and hospital personal are informed of the need for UV protection.

Due to good UV protection and improved medical care, XP patients are living longer and increasingly more public lives. Planning for college and careers is something that XP patients and families now need to consider. XP patients can work at jobs that do not involve prolonged day-time outdoor activities. Adult XP patients enrolled in the NIH natural history study (1, 19) hold positions such as physician assistant, computer scientist, and flooring business owner. These patients are able to be active in the community while maintaining an adequate level of UV protection (22–24).

XP is a serious condition with life-limiting consequences. However, with early diagnosis, the advent of new techniques to shield XP patients from UV, and the practical knowledge gained from patients and families living with XP, more patients are living full, active, socially interactive lives. Lessons learned by photoprotection of XP

patients may be useful for patients with other very photosensitive disorders.

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