



# XERODERMA PIGMENTOSUM

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Xeroderma pigmentosum (XP) is a rare disorder transmitted in an autosomal recessive manner. It is characterized by photosensitivity, pigmentary changes, premature skin aging, and malignant tumor development. These manifestations are due to a cellular hypersensitivity to ultraviolet (UV) radiation resulting from a defect in DNA repair. The frequency of XP in the United States is approximately 1 case per 250,000 and the disease is usually detected at age 1-2 years. The basic defect in XP is in nucleotide excision repair (NER), leading to deficient repair of DNA damaged by UV radiation. Seven XP repair genes, XPA through XPG, have been identified.

A history of severe persistent sunburn can be found in many patients. The history should focus on the relationship of the eruption to sun exposure, with a careful determination of its time course and morphology. As with most autosomal recessive disorders, usually no family history is present; the parents, being heterozygotes, are healthy. Moreover, a history of consanguinity may be elicited. The disease typically passes through 3 stages. The skin is healthy at birth. Typically, the first stage appears after age 6 months. This stage is characterized by diffuse erythema, scaling, and freckle-like areas of increased pigmentation. These findings are seen over light-exposed areas, appearing initially on the face. With progression of the disease, the skin changes appear on the lower legs, the neck, and even the trunk in extreme cases. While these features tend to diminish during the winter months with decreased sun exposure, as time passes, these findings become permanent. The second stage is characterized by poikiloderma. Poikiloderma consists of skin atrophy, telangiectasias, and mottled hyperpigmentation and hypopigmentation. Although telangiectasias also occur in the sun-exposed areas, they have been reported to arise in unexposed skin and even buccal mucosa. The third stage begins by the appearance of numerous malignancies, including squamous cell carcinomas, malignant melanoma, basal cell carcinoma, and fibrosarcoma. These malignancies may occur as early as age 4-5 years and are more prevalent in sun-exposed areas.

Photosensitivity should be suspected and evaluated in any patient with intermittent or persistent abnormalities on light-exposed areas. Ocular problems occur in nearly 80% of individuals with XP; the initial problems include photophobia and conjunctivitis. Neurologic problems are seen in nearly 20% of patients with XP, more commonly in groups XPA and XPD. The problems include microcephaly, spasticity, hyporeflexia or areflexia, ataxia, chorea, motor neuron signs or segmental demyelination, sensorineural deafness, supranuclear ophthalmoplegia, and mental retardation. The neurologic problems might overshadow the cutaneous manifestations in some patients with XP. De Sanctis-Cacchione syndrome refers to the combination of XP and neurologic abnormalities (including mental retardation and cerebellar ataxia), hypogonadism, and dwarfism.

No consistent routine laboratory abnormalities are present in XP patients. The diagnosis of XP can be established with studies performed in specialized laboratories. These studies include cellular hypersensitivity to UV radiation and chromosomal breakage studies, complementation studies, and gene sequencing to identify the specific gene complementation group. Prenatal diagnosis is possible by amniocentesis or chorionic villi sampling. The goal of treatment is to protect the patient from sunlight. To this end, regular visits to the dermatologist might be necessary for the purposes of patient education and early detection and treatment of any malignancies. Gene therapy for XP is still in a theoretical and experimental stage. Consultation with an ophthalmologist and a neurologist is recommended because of the ocular and neurologic problems associated with XP.

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