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Burning issues in the diagnosis of xeroderma pigmentosum

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Xeroderma pigmentosum (XP) is a rare (about 1 per million)¹ autosomal recessive genodermatosis with a high frequency of sunlight-induced skin cancers in association with defective DNA repair. Most patients with XP develop multiple freckle-like lentiginous lesions on sun-exposed skin at an early age. Patients with XP generally present in two different ways.² Some have an exaggerated response to ultraviolet radiation (UVR) with severe burning on minimal exposure. Others have a normal acute response to sun exposure. In the general population, burning after sun exposure is a risk factor for melanoma and nonmelanoma skin cancer (NMSC).

A long-term follow-up of the 106 patients with XP admitted to the U.S. National Institutes of Health (NIH) between 1971 and 2009 found an approximately 2000-fold increase in melanoma and a 10 000-fold increase in NMSC in patients with XP younger than 20 years of age.³ The 22-year median age at diagnosis of first melanoma was significantly older than the 9-year median age at diagnosis of first NMSC, a relative age reversal from the general population suggesting different mechanisms of carcinogenesis between melanoma and NMSC. Slightly more than one-third (36%) of these patients with XP had a history of never burning after sun exposure. These patients were in XP complementation groups C, E and variant. Surprisingly, these patients with XP had an earlier age of onset of skin cancer than the patients with XP (in complementation groups A and D) who had a history of always or sometimes burning. The NIH researchers suggested that this may be related to the extreme sun protection that the patients with XP who burn on minimal sun exposure receive from an earlier age, decreasing their total UVR exposure.

A multidisciplinary clinic for the evaluation and treatment of patients with XP was recently established at St John's Institute of Dermatology in London. Headed by a dermatologist, Dr Robert Sarkany, the clinic includes specialists in ophthalmology, neurology, surgery, dermatopathology, radiology and photography. Their affiliated nurses are able to make home visits to evaluate patient care. The DNA Repair Group in Sussex performs laboratory testing of the patients. They work closely with support groups for patients with XP and serve as the XP clinic for the whole of the U.K.

In a relatively short time the London group evaluated 60 patients with XP. They established a simple three-point scale for retrospective evaluation of sun sensitivity and classified the

patients. In the current issue of the BJD⁴ they report that about half of these patients with XP did not have a history of acute burning on minimal sun exposure. Like the NIH patients, these patients were in XP complementation groups C, E and variant, and had an earlier age of onset of skin cancer than the patients with XP who burned on minimal sun exposure. Both research groups indicated that the patients with XP who burned on minimal sun exposure had an increased risk of development of XP neurological degeneration. The NIH researchers recently reported that standard audiograms may serve as an additional predictor of patients with XP who may develop neurological degeneration.⁵

Sun-induced lentiginous hyperpigmentation under the age of 2 years should raise suspicion for a diagnosis of XP. Acute burning on minimal sun exposure can support this diagnosis but this sun reaction may be absent in one-third to one-half of patients with XP.

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