Outdoor sports and risk of skin lesions

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MADAM, With interest we read the study by Mahé *et al.*[1] about the difference in the number of ultraviolet (UV) radiation-related skin lesions in children playing outdoor sports and children who did not. Indeed, as the incidence of UV radiation-related skin lesions is increasing, it is important to identify risk factors in order to guide preventive actions. However, we have reasons to believe that the study design prohibits drawing the conclusion that 'outdoor sports increase the risk of developing UV radiation-induced skin lesions in childhood'.

As data about sport activities were only collected in 2009, the design of this study is essentially cross-sectional. With this design it is only possible to show an association between UV radiation-related skin lesions and outdoor sports, and not the causal relation which is implied by the authors.

This is especially of importance as the authors did not control for any confounders in their analysis (e.g. skin colour, playing outside). Therefore, other factors may have played a substantial role in the association between outdoor sports and UV radiation-related skin lesions, and the difference found may be overestimated. Furthermore, the assumption that 'children who practised at least one sport always or sometimes played outside' may be too optimistic.

Future studies should therefore not focus on larger groups, as suggested by the authors, but rather on a different study design, for example a cohort study. Regular follow-up moments should be planned to determine the frequency and degree of outdoor sports, so that the true relation between outdoor sports and UV radiation-induced skin lesions can be determined.

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1 Mahé E, Beauchet A, de Paula Corrêa M *et al.* Outdoor sports and risk of ultraviolet radiation-related skin lesions in children: evaluation of risks and prevention. *Br J Dermatol* 2011; **165**:360–7.

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Possible role of interleukin-17 in the pathogenesis of lichen planus

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MADAM, Lichen planus (LP) represents a mucocutaneous inflammatory disease of unknown aetiology. Skin lesions of LP are characterized by a subacute or chronically progressive appearance of polygonal papules. Oral lesions present with bilateral white striations or plaques on the buccal mucosa, tongue and gingivae. LP shows apoptosis of keratinocytes, acanthosis, hypergranulosis, and a lymphocytoid cell-rich infiltrate in the upper dermis.[1]

T-helper (Th) cells may differentiate into two major subtypes with distinct cytokine profiles and functions in the immune system. Th1 cells typically produce interferon-γ and tumour necrosis factor-α, which are involved in macrophage activation and play a role in autoimmune disease associated with chronic infections. Th2 cells produce interleukin (IL)-4, IL-5 and IL-13 and play a role in allergic diseases and defence against helminthic parasites. A third subset is called the Th17 because its signature cytokine is IL-17. Several studies have investigated the role of Th1 and Th2 cells and their cytokines in the pathogenesis of LP.[2] We attempted to investigate the possible role of IL-17 in LP. Thirty patients with LP and 20 age- and sex-matched healthy controls were included in this study. All patients were subjected to full history taking including age, sex, disease duration, body surface area involved and associated viral hepatitis. Serum IL-17 was measured by enzyme-linked immunosorbent assay technique (BioSource Europe SA, Nivelles, Belgium).

Patients' ages ranged from 16 to 68 years. The duration of LP ranged from 3 weeks to 17 years with extent of LP ranging from 1% to 30% (Table 1). Twenty per cent of the patients had viral hepatitis. Fifteen patients had previously received therapy for LP (topical corticosteroids in 12 patients, systemic corticosteroids in three patients).

Mean ± SD serum IL-17 level was 19·76 ± 4·31 pg mL^{-1} in patients with LP and 5·26 ± 1·45 pg mL^{-1} in controls. This

Table 1 Characteristics of patients enrolled in the study

	Patients (n = 30)	Controls (n = 20)
Age (years), mean ± SD (range)	42·7 ± 15·4 (16–68)	28·4 ± 8·2 (18–45)
Men/women	16 (53%)/14 (47%)	6 (30%)/14 (70%)
Disease duration, mean ± SD (range)	3·3 ± 5·4 years (3 weeks–17 years)	–
Extent of disease (%), mean ± SD (range)	9·6 ± 8·0 (1–30)	–

Table 2 Comparison of serum interleukin (IL)-17 levels in patients with lichen planus

Characteristic	n	Serum IL-17 (pg mL^{-1}), mean ± SD	P-value
Male	16	19·6 ± 2·98	NS
Female	14	19·9 ± 5·57	
Positive viral hepatitis	6	20·1 ± 1·39	NS
No associated viral hepatitis	24	19·5 ± 4·80	

NS, not significant ($P > 0·05$).

difference was statistically significant. There was no statistically significant difference in serum IL-17 levels as regards gender, age, disease duration, extent of LP or history of viral hepatitis (Table 2).

The aetiology of LP remains unclear. A delayed hypersensitivity immune reaction, in which the release of cytokines by activated T cells leads to the attraction of inflammatory cells and to the destruction of keratinocytes by cell-mediated cytotoxicity, has been implicated in the pathogenesis of LP.[3] In LP, the lymphocytic infiltrate is composed almost exclusively of T cells, and most T cells within the epithelium/epidermis and adjacent to damaged basal keratinocytes are activated CD8+ lymphocytes. Most intraepithelial lymphocytes in LP are CD8+ cytotoxic T cells, and most lymphocytes in the connective tissue are CD4+ helper T cells.[4,5] The abundance of such T-cell infiltrate in LP further supports the participation of cellular immunity with both helper and cytotoxic T cells playing a vital role in the pathogenesis of LP. Previous studies have described the expression pattern of the different cytokines/chemokines, which involved a Th1 and/or Th2 polarization, in tissues and serum from patients with LP. Sugerman *et al.*[4] concluded that LP was characterized by a Th1 cytokine bias. Rhodus *et al.*[6] concluded that different patterns of Th1/Th2 imbalance, with Th1 overactivation or mixed Th1/Th2 conditions, may occur in oral LP. Recent studies indicate that the cytokine IL-17 is the major mediator of tissue inflammation in several autoimmune and inflammatory diseases and its expression has been detected in sera and tissues in rheumatoid arthritis, multiple sclerosis and systemic lupus erythematosus.[2]

We found that the serum levels of IL-17 were significantly higher in patients compared with controls. IL-17 can contribute in the pathogenesis of LP by enhancing T cell-mediated reactions and inducing production of chemokines and other cytokines. Other mechanisms have been implicated in the pathogenesis of LP including mast cell degranulation and matrix metalloproteinase (MMP) activation. IL-17 has been shown to upregulate and/or synergize with local inflammatory mediators and promote extracellular matrix injury through stimulation of production of MMP.[7] Th17 cells may arise during immune responses against extracellular pathogens and fungal infections in mice as well as humans.[8,9] The increase of serum levels of IL-17 in patients with LP is of special interest, knowing the association of this disease with infections. Th17 responses have been reported in hepatitis C infection which in turn has been associated with LP.[9] In this study, there was an increased level of IL-17 in patients with LP including those with a history of underlying viral hepatitis infection. This increase was not significant when compared with other patients with LP with a negative history for viral hepatitis. The exact link between the increased levels of IL-17 in viral hepatitis and LP is yet to be determined.[10]

In conclusion, this is the first study that suggests a possible role of IL-17 in the pathogenesis of LP and may support a hypothesis that shifting of the immune system towards a Th17 response may be involved in LP.

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