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Siblings of melanoma patients screened

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Melanoma is a treatable, lethal disease that can be almost 100% curable if discovered soon enough. Siblings of melanoma patients have been targeted in a recent intervention program to educate people on the dangers of melanoma and encourage screening for the disease, which was published in the August 2006 issue of *Cancer*. There are over half a million siblings of patients diagnosed with melanoma that are between two- and eight-times more likely to develop it themselves.

The intervention, led by Alan Geller (University School of Medicine, MA, USA), consisted of four parts and addressed originally 495 siblings, of whom 403 continued in the program for at least 6 months. The siblings were randomly assigned to two groups. The first group received the four-part intensive education program, whilst the other received standard care. All were observed for 12 months. This was the first study that compared the impact of intervention in melanoma awareness and prevention in high-risk groups.

The initial phase of the education was a motivational, goal-setting session with the health educator via telephone. The second stage involved the siblings receiving three sets of specifically selected computer-generated material that was followed by the third stage of three telephone counselling sessions. The final stage consisted of referrals to free screening sessions.

The Boston-based study showed clearly that the education program led to an improved likelihood of self-skin examination. The siblings who underwent the education program were more likely to examine all moles, including moles on the back. Both groups showed the same results for the use of sunscreen (two thirds) and there was no difference between the two groups for skin cancer examinations from a physician.

Previously, despite the higher risk of developing the disease, siblings have not taken part in self-screening or been screened by physicians. They (and this was the practice of the control arm) are informed, currently, by their sibling who has been diagnosed with melanoma to see their physician. The researchers hope that this study 'may provide a useful foundation for future efforts to target the more than half million siblings at risk from melanoma'.

Eczema affects quality of life in children as much as kidney disease

The impairment of quality of life of a child suffering from a skin disease is similar to that of a child suffering from a chronic illness, revealed a study published in the July issue of the *British Journal of Dermatology*.

"Our study shows that children with chronic skin diseases – and their parents – reported the same level of quality of life impairment as the parents of children with many other chronic illnesses", reports Paula Beattie (Royal Hospital for Sick Children, Glasgow, UK).

The researchers quizzed sufferers of diseases, such as acne, psoriasis and eczema – in total 379 children aged 5–16 years and their parents over a 6-month period. The participants were interviewed and results compared using health-related quality of life (HRQL) measures. These measures allow comparisons of different diseases and a comparison with normal life via numerical values. For this study, a new generic form of a HRQL was used – the Children's Life Quality Index (CLQI). This was cross-validated with a pre-established speciality-specific dermatological questionnaire, the Children's Dermatology Life Quality Index (CDIQL). The results were compared with those of 161 sufferers of chronic diseases, such as cystic fibrosis and renal disease.

The participants were asked about the effect on the quality of the child's life in respect to factors, such as pain, teasing, loss of sleep, dietary restrictions and medical treatment. The children gave their results using the established CDIQL, while the parents of both groups answered questions with respect to the CLQI. The study also wanted to compare the CDIQL results with the CLQI to validate the HRQL proxy measure.

To ascertain a relationship between the CLQI and the CDLQI scores, the results were analysed using linear regression and displayed a clear linear association ($rs = 0.72$; $p < 0.001$). The two results also showed promising agreement using the Bland–Altman plot (expressing scores out of 100, the 95% limits of agreement were from -25.5 out of 100 to 26.7 out of 100).

Both renal disease and eczema were seen to give a 33% impairment on life by parents. Children rated psoriasis and atopic dermatitis as the most life impairing (CDLQI = 30.6 and 30.5%, respectively) with respect to skin complaints. The CLQI scores from parents rated cerebral palsy with the highest score (38%). Next was renal disease and atopic dermatitis, followed by cystic fibrosis (32%), urticaria and asthma (both with 28%), psoriasis (27%), epilepsy (24%), diabetes, alopecia and localized eczema (all with 19%). The least impairing of those studied was acne (16%).

Beattie and her team emphasized that skin diseases do not shorten life as serious conditions do, but they cause the same amount of distress in everyday life. "Some skin conditions can also disturb children's sleep and cause lack of

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self-confidence, embarrassment and poor self-esteem, especially as they get older." The study also highlighted that skin conditions were more clearly visible than other conditions. "Skin diseases are often more obvious to children than chronic diseases such as asthma or diabetes and are more likely to lead to alienation, name calling, teasing and bullying."

The researchers believe that their findings will be important in recognizing the detrimental effects of skin disorders and emphasizing the need for vital resources. Previously, it has been a common misconception that dermatological diseases have less of an impact on a patient's life than other, more serious, diseases. The results from this study give a good insight of the impact of such diseases from the patient's perspective.

"Our study clearly shows the profound effect skin disease can have on a children's quality of life and we hope that our findings will raise awareness of the problems they face and encourage greater sensitivity towards them", concluded Beattie.

Fibroblast growth factor receptor 3 gene mutation linked to epidermal nevi

The genetic basis for epidermal nevi may have been recently discovered. Christian Hafner and coworkers (University of Regensberg, Germany) believe that the problem may arise from an embryonic mutation of the fibroblast growth factor receptor 3 (*FGFR3*) gene.

The disease affects approximately one in 1000 people but the study, to appear in the August edition of the *Journal of Clinical Investigation,* describes results that could lead to an effective treatment.

The team examined the epidermal nevi of 33 patients and, in 33% of these, the cause of the thickened skin was activating point mutations, almost exclusively at codon 248 (RZ48C), of *FGFR3* in the human epidermis. This was caused by an embryonic mutation. The team screened the epidermal nevi using a SNaPshot multiplex assay for 11 activating *FGFR3* point mutations.

Epidermal nevi syndrome, a multisystem neurodermatological disorder, may be associated with neurological, skeletal or ocular malignancies and other cutaneous disorders. The research team discovered that mutations of *FGFR3* result in autosomal dominant skeletal disorders, such as achondroplasia, which may be associated with dermal acanthosis nigricans. Acanthosis nigricans share some of its clinical and histological features with nonorganoid, nonepidermolytic common epidermal nevi.

These findings offer hope to sufferers of the potentially disfiguring congenital skin lesion as molecular-targeted inhibitors for the *FGFR3* gene already exist. A topical solution could therefore prove to be a promising noninvasive treatment.

Psoriasis treatments compared

The efficacy of two chronic plaque psoriasis treatments – psoralen UVA (PUVA) and narrowband UVB (NB-UVB) – have been compared in a head-to-head trial. In the study by Sami Yones and colleagues at Kings College London, UK, PUVA proved to be the more effective treatment in clearing the inflammatory condition with fewer treatments and with longer lasting results.

Plaque psoriasis is the most common type of the inflammatory condition with approximately 80% of diagnosed psoriasis cases being of this variety. The plaques appear as red raised skin that is covered by a silvery white scale. These plaques can occur anywhere on the body but appear most commonly on elbows, knees, the lower back and the scalp. The findings, reported in the July issue of *Archives of Dermatology,* clearly show that PUVA is the treatment of choice for this condition.

A total of 93 chronic plaque psoriasis sufferers were assigned to two groups in the double-blind randomized study to compare the two treatments. Both groups were treated with their chosen treatment twice weekly. This continued up to 30 sessions of treatment or until the psoriasis ceased to persist. The patients who recovered during the study were then observed for the following 12 months or until they suffered a relapse.

The administered dose began at 70% of the minimum phototoxic or erythema dose and was increased by an increment of 20%. The results focused on the percentage of patients who achieved clearance of the disease, the number of treatments required until clearance and (if clearance occurred) the percentage remaining in remission after 6 months.

In patients with skin types I–IV, PUVA showed to be significantly more efficacious than NB-UVB at attaining clearance (84 vs 65%; $p = 0.001$). For clearance completion in PUVA, a median of 17 treatments were required compared with 28.5 for NB-UVB. The 6-month follow-up of patients who had achieved clearance showed that 68% of PUVA-treated patients remained in remission as were 35% of NB-UVB-treated patients. The clearance rate for patients who had skin types V and VI was 24% compared with 75% for patients with skin types less likely to burn.

Although the results clearly indicated that PUVA was more effective than NB-UVB, 49% of patients being treated this way suffered erythema compared with 22% in the NB-UVB group. The difference, the group claims, "could have been due to ascertainment bias". Other disadvantages of PUVA include nausea and a potential to cause skin cancer; it also cannot be used in pregnancy.

Yet, despite these concerns over PUVA, the team urge that it "tends to clear psoriasis more reliably, with fewer treatments and for longer, and should, therefore, still be used in appropriate patients."

New results prevent overdiagnosis of melanoma

Results from the University of Pittsburgh (PA, USA) distinguish sun damage from *in situ* melanoma by quantifying the expected melanocytes in sun-exposed caucasians. Previously, there was no such method.

"There are many uncertainties in medicine. In many instances these uncertainties lead to overly aggressive treatments", explains Ali Hendi (Mayo Clinic, FL, USA), who led the study. "We didn't have an accurate way to distinguish cancer from overexposed, but normal, skin, and this study was designed to find the missing link."

The Pittsburgh-based team believed that surgeons may have been overdiagnosing in instances where they mistook sun-damaged skin for melanoma, which resulted in unnecessary surgery in which complications or deformity could arise. The team ascertained the density, confluence and depth of follicular penetration of melanocytes in face and neck skin that had long-standing sun exposure.

The study was based on results from 149 randomly selected patients, all of whom had undergone Mohs surgery of the face and neck for basal cell and squamous cell carcinoma during a 5-month period starting in December 2003. The team looked at normal but sun-damaged tissue that had been discarded after the tumors were removed. Frozen section slides were taken and stained with melanoma antigen recognized by T cells-1 immunostatin.

The team determined the density, confluence and depth of follicular penetration of melanocytes per high power field and using × 400 magnification – equivalent to 0.5 mm of skin. The confluence was categorized depending on how many adjacent melanocytes there were (0–1 = none, 2 = mild, 3–6 = moderate and >6 = severe).

Results from the study, published in July issue of *Archives of Dermatology,* showed that the range of melanocytes was 6–29, with the mean being 15.6. The confluence was none for 11%, mild in 54%, moderate in 34% and severe in 1% of those included. The mean depth of melanocyte follicular epithelium penetration was 0.38 mm. Pagetoid spread and nesting of melanocytes were not seen.

Areas of increased melanocyte density were seen in 24.2% of patients and these areas were also examined closely. These focal areas showed the mean number of melanocytes to be 20.3 (range: 7–36), a severe classification of confluence in 13.0%, moderate in 50.0% and mild in 37.0%.

Melanoma, the deadliest form of skin cancer, can now be distinguished from normal skin by several factors discovered by the team. Previously, this proved difficult. Unnecessary surgery can now be avoided as surgeons now know that absence of pagetoid spread or nesting, increased melanocyte density and moderate confluence are all normal in long-standing sun-exposed skin.

"To be able to look in the microscope and have a measurement by which to determine successful removal of melanoma *in situ* is something that we've hoped for quite a while", explains Hendi. "In many cases, surgeons can stop removing tissue much sooner, which will result in less trauma to the skin."