INTRODUCTION

Melanocytic nevi are benign clusters of melanocytic nevus cells arising as a result of proliferation of melanocytes at the dermo-epidermal junction. These may all remain in contact with the basal layer of the epidermis, giving rise to the junctional nevus. In other nevi, some of the nevus cells may migrate into the dermis over time, giving rise to the compound nevus. The end stage of this process is when there is no nevus cells attached to the epidermis and all are lying free in the dermis. This pattern is that of the mature intradermal nevus. A melanocytic nevus is therefore a benign tumor of melanocytes, in which the melanocytes (nevus cells) proliferate for some time but then cease proliferation and differentiate and come to resemble cells of neural or fibroblast lineage ***(Newton Bishop, 2010).***

Melanocytic nevi develop through childhood and twin studies provide good evidence that nevus number is predominantly genetically determined ***(Zhu et al., 1999)*** with a smaller effect of sun exposure ***(Wachsmuth et al., 2005)***. There are a number of studies from Europe and Australia, which suggest that nevus number is higher in children exposed to more sun, particularly intermittent sun exposure as on sunny holidays ***(Gefeller et al., 2007) (Rodvall et al., 2007).***

Recognition in 1980s that the number of melanocytic nevi strongly influences the risk of melanoma prompted researchers to study the epidemiology of nevi, particularly in children. Common acquired nevi are nevi that are absent at birth, often present in the early years of childhood, and present in greater numbers in early to middle life and do not multiply thereafter ***(Greene et al., 1985).***

Cross-sectional studies suggest that childhood is the most important time for the formation and evolution of nevi ***(Oliviera et al., 2009).***

Vredenborg et al. stated that Numbers and distribution of melanocytic nevi in childhood are major indicators of the risk of melanoma in patients from families with familial melanoma ***(Vredenborg et al., 2014).***

Exposure to ultraviolet light is the major environmental factor for malignant melanoma and ultraviolet protection is most critical in pre-school children. Sun protection should focus on those anatomical regions with the highest increase in melanocytic nevi, i.e face, ears and lower arms ***(Wollina et al., 2014).***

There is mounting evidence suggesting that the morphological subtypes of nevi are also age-dependent ***(Zalaudek et al., 2009).***

It must be acknowledged that the classification of melanocytic nevus subtypes is an evolving science ***(Zalaudek et al., 2006b)***

Currently, there are different classification schemes that are dependent on the method of obtaining morphological information. While clinical (non dermoscopic) classification involves flat, elevated and nodular types, dermoscopy identifies globular, reticular or structureless morphologies, with various combinations of these features as subtypes ***(Argenziano et al., 2007a)*.**

Ackerman and Magana-Garcia 1990 proposed a scheme based on the histological criteria of flat (Clark's, junctional or compound), exophytic (Miescher's, intradermal) and endophytic (Unna's, intradermal) nevi.

It is surprising that most studies investigating age related nevus patterns report similar results, irrespective of the scheme used to classify nevi. There is a high prevalence of intradermal and compound nevi in both children and the elderly ***(Martinka et al., 2007b)*** dermoscopically characterized by a globular or structureless pattern ***(Zalaudek et al., 2006a)*** whereas adults have reticular, predominantly intraepithelial (junctional-superficial compound) nevi ***(Westhafer et al., 2007)*.**

These age-related differences in nevus patterns between children and adults has led to the hypothesis that nevogenesis

occurs by two distinct pathways. One, the congenital or constitutional pathway, gives rise to globular-structureless nevi with onset during childhood. These nevi are thought to derive from predominantly dermal melanoblasts (i.e. not fully mature melanocytes) and represent persisting small congenital nevus-like proliferations that acquire the typical appearance of an intradermal nevus with time. In contrast, the acquired or exogenous pathway is responsible for the formation of reticular nevi (i.e. flat, Clark's nevi). It is hypothesized that these nevi derived from predominantly intraepidermal melanocytes (i.e. mature melanocytes), which proliferate in response to factors such as intermittent UV light exposure ***(Zalaudek et al., 2007b).***

Dermoscopy is a noninvasive technique that allows the visualization of subsurface structures by decreasing reflection at the stratum corneum-air interface. Recognition of these structures has led to the introduction of clinical criteria for the assessment of pigmented lesions ***(Argenziano et al., 2003)*** and enabled a detailed classification of nevi based on their global dermoscopic pattern ***(Hofmann-Wellenhof et al., 2001).***

A dermoscope is considered a "stethoscope" for a dermatologist and the two important features of dermoscopy that differentiate melanoma from a melanocytic nevus are an asymmetry of colours and an asymmetry of structures, but not an asymmetry of contour (shape). It should be borne in mind that, many benign nevi are not completely symmetrical

concerning the contour and there is more or less some degree of irregularity. Dermoscopy helps to clarify this point and illuminates the diagnostic features of colour distribution and structural symmetry ***(Tanaka 2013).***

Types of dermoscopy devices are:

- Non polarized light contact dermoscopy, this device uses non polarized light source (a halogen light source at a 45° angle), and requires the use of an oil or gel interface on the lesion to prevent surface reflection.

- Polarized contact/noncontact dermoscopy which do not need a liquid interface and are equipped with a cross-polarized lens that absorbs scattered light waves ***(Goodson and Grossman 2009).***

- Combined polarized and non polarized dermoscopy, these devices incorporate the desirable characteristics of both types of dermoscopy ***(Marchionda et al., 2010).***

Longitudinal studies of dermoscopic patterns of nevi have been performed in adults, mostly in patient populations at high risk for melanoma. However, population-based studies of dermoscopic patterns and, specifically, studies of dermoscopic nevi patterns in children are still scant, but are essential to improve our understanding of Nevogenesis ***(Haenssle et al., 2006).***

AIM OF THE WORK

The aim of this work is to study the characteristics of the predominant dermoscopic pattern of melanocytic nevi in prepubertal children of our population and to relate it to constitutional factors.

Chapter (1)

DERMOSCOPY

Dermoscopy is a non invasive method that allows the in vivo evaluation of colors and microstructures of the epidermis, the dermo-epidermal junction, and the papillary dermis which are not visible to the naked eye. These structures are specifically correlated to histologic features. The identification of specific diagnostic patterns related to the distribution of colors and dermoscopy structures can better suggest a malignant or benign pigmented skin lesion (PSL). The use of this technique provides a valuable aid in diagnosing PSLs. Because of the complexity involved, this methodology is reserved for experienced clinicians ***(Stanganelli et al., 2008).***

Over the past years, dermoscopy has been known by a variety of names, including skin surface microscopy, epiluminescence microscopy (ELM), incident light microscopy, dermatoscopy, and video dermatoscopy. The term "dermoscopy," however, first used by ***Friedman et al. in 1991***, enjoys the greatest international consensus ***(Argenziano et al., 2003).***

Dermoscopy became more widespread in the 1990s. To the present day, dermoscopy is used in assessing inflammatory dermatoses (inflammoscopy), parasitic invasions (the so-called "entomodermoscopic method") and in cases of scalp disorders

(Trichoscopy) -all in the follow-up to dermatological treatment. Performing dermoscopy during dermatological examination should really be adapted as a routine activity. Although a complete and thorough examination of the skin with the use of a dermoscope is, effectively, more time-consuming, it is strongly advisable to dedicate the incurring three or four additional minutes (compared to a traditional dermatological examination without the use of dermoscopy) to increase the detection sensitivity of potentially fatal skin malignancies ***(Zalaudek et al., 2008a).***

Historical Background

Skin surface microscopy started in 1663 with Kolhaus who investigated the small vessels in the nail fold with the help of a microscope ***(Soltz et al., 2002).***

In 1878, Abbe described the use of immersion oil in light microscopy and this principle was transferred to skin surface microscopy by the German dermatologist, Unna, in 1893. He introduced the term ‘‘diascopy’’ and described the use of immersion oil and a glass spatula for the interpretation of lichen planus and for the evaluation of the infiltrate in lupus erythematosus ***(Carli et al., 2001)***.

The term ‘‘dermatoscopy’’ was introduced in 1920 by the German dermatologist Johann Saphier who published a series of communications using a new diagnostic tool

resembling a binocular microscope with a built-in light source for the examination of the skin. He used this new tool in various indications and did some interesting morphological observations on anatomical structures of the skin which indicated the high performance of his equipment ***(Kenet et al., 1993).***

Goldman in 1951 developed the first portable dermoscope, and analyzed nevi and melanoma with monocular devices in the United States. He published a series of interesting articles on new devices on what he called ‘‘Dermoscopy’’. He was the first dermatologist to use this new technique for the evaluation of pigmented skin lesions.

Mackie (1971) clearly identified, for the first time, the advantage of surface microscopy for the improvement of preoperative diagnosis of pigmented skin lesions and for the differential diagnosis of benign versus malignant lesions. These investigations were continued mainly in Europe by several Austrian and German groups.

Progress in dermoscopy went faster where ***Fritsch and Pechlaner in 1981*** distinguished benign from malignant skin lesions according to the characteristics of the pigmented net of the lesions. ***Pehamberger et al. 1987*** introduced the analysis of patterns for the diagnosis of pigmented cutaneous lesions. ***Soyer et al. (1989)*** established a correlation between dermoscopic and histopathologic structures. In the same year,

the 1st Consensus Conference on Skin Surface Microscopy was held in Hamburg, Germany where a terminology for dermoscopy was defined. ***In 1990 Kreusch and Rassner*** published the first Dermoscopy Atlas.

From the 1990s onwards, several dermatology research groups developed several different diagnostic methods for analyzing dermoscopic images. At the same time hand held dermoscopes became widely commercially available for purchase enabling an increased uptake in their use around the world ***(Peris et al., 2002).***

From the year 2000 to the present, interest in this technology has been increasing, with the global spread of dermoscopy and the production of several courses, books, publications, and symposia on the theme, as well as the founding of the International Society of Dermoscopy ***(Stolz et al., 2002; Rezze et al., 2004; Ferreira et al., 2004).***

Scientific background*:*

The basic principle of dermoscopy is transillumination of a lesion and studying it with a high magnification to visualize subtle features ***(Stolz et al., 1994).*** Normally, light is reflected, dispersed or absorbed by the stratum corneum due to the differences in refractive index and optical density between skin and air. Thus, the skin appears opaque and the underlying structures cannot be adequately examined ***(Kenet et al., 1993).***

Most of the light incident on dry, scaly skin is reflected, but smooth, oily skin allows most of the light to pass through it, reaching the deeper dermis. This principle has been harnessed to improve the visibility of subsurface skin structures by employing application of linkage fluids over the lesions to be studied to improve the translucency of the skin (Fig. 1). Various linkage fluids used are oils (immersion oil, olive oil and mineral oil), water, antiseptic solutions and glycerin. Immersion oil is not used anymore because it contains chlorinated paraffin and dibutyl phthalate which have teratogenic, fetotoxic, and carcinogenic effects ***(Nischal and Khopkar, 2005).***

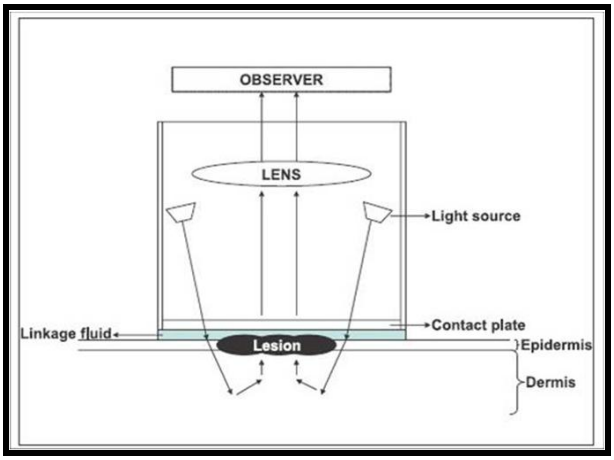

Figure (1): Optics of dermoscope. Adapted from ***(Nischal and Khopkar, 2005)***.

Water or antiseptic solutions evaporate quickly and hence are less preferred than oils. Liquid paraffin has been used, which is inexpensive, safe and easily available, with good results. Glass has a refractive index (1.52) similar to that of skin

(1.55) and hence when placed over oil-applied skin, further enhances transillumination of the lesion ***(Rabinovitz, 1998).***

Alcohols, due to their low viscosity, amphipathic properties, disinfectant capabilities and most importantly image clarity, are the best immersion liquids to use. 70% ethanol is chosen in offices because it has fewer odors than isopropanol and does not leave crystal deposits after evaporation like alcoholic disinfectants containing chlorhexidine ***(Katz and Rabinovitz, 2001).***

New hand-held dermoscopes are now available on the market that are provided with polarized light, rendering the fluid placed on the lesion unnecessary for inspecting pigmented skin structures ***(Nischal and Khopkar, 2005).***

Components of a dermoscope:

The essential components of a dermoscope are:

a) Achromatic lens: Most instruments provide 10 x magnifications, but higher magnifications can be achieved with special lenses ***(Pehamberger et al., 1987).***

b) Inbuilt illuminating system: Halogen lamps, which are oriented at an angle of 20 degree, are placed within the handheld piece. The colour contrasts of lesions are altered by the yellow light of halogen lamp. Light emitting diodes (LED) (Delta 20©, Derm Lite©) provide high intensity

white light and consume 70% less power than halogen lamps. Illumination can be altered by turning off a set of LEDs. They are also designed to emit lights of different colors for better visualization of the skin as penetration of the skin by light is proportional to the wavelength of light (Derm Lite MS©) ***(Nischal and Khopkar, 2005).***

c) Power supply: Handheld instruments are usually powered by batteries, e.g. lithium ion battery, rechargeable lithium battery, AA battery, and rechargeable handles ***(Mayer, 1997).***

Additional facilities in some dermoscopes are an inbuilt photography system either an attachable conventional or digital camera or an inbuilt camera, and supporting software, for the capture, storage, retrieval and even interpretation of images ***(Kittler et al., 2002).***

Types of dermoscopy devices are as follows*:*

• **Non polarized light contact dermoscopy.** This device uses a non polarized light source (a halogen light source at a 45° angle), and requires the use of an oil or gel interface on the lesion to prevent surface reflection. It provides better illumination and resolution than polarized dermoscopy. The colors of lesions appear sharper in non polarized dermoscopy compared with polarized dermoscopy; the former is therefore useful in visualizing milia-like cysts and comdeo-like openings,

peppering, lighter colors, and blue-light areas ***(Goodson and Grossman, 2009).***

• **Polarized contact/noncontact dermoscopy.** Polarized dermoscopy devices do not need a liquid interface and are equipped with a cross-polarized lens that absorbs scattered light waves. Polarized contact dermoscopy can attain the images of vascular and other deeper structures, and is a useful tool in visualizing melanin, blue nevi, and shiny white streaks. Polarized noncontact dermoscopy is better used for imaging mucous membranes. Since direct skin contact is not required for visualization, the use of noncontact dermoscopy minimizes the risk of nosocomial infection ***(Wang et al., 2008).***

• **Combined polarized and non-polarized dermoscopy.** These devices incorporate the desirable characteristics of both types of dermoscopy. Clinicians can choose to use either polarized or non-polarized lights ***(Marchionda et al., 2010).***

Theoretical Advantages*:*

Because of its ability to magnify lesions and reveal subsurface structures, dermoscopy is expected to have higher sensitivity and specificity than the naked eye in detecting malignancies, thus increasing the number of melanomas that are identified and sent for biopsy, while reducing the number of unnecessary biopsies. It may even allow melanomas to be

identified at earlier stages which could lead to better outcomes ***(Carli et al., 2004).***

The use of dermoscopy may help to allay patient anxiety as one survey reported that more than half of the dermatologists queried responded that dermoscopy was effective in reducing patients' anxiety ***(Noor et al., 2009).***

Theoretical Disadvantages*:*

The use of dermoscopy requires training and this may be considered a theoretical disadvantage for those who are not willing to invest in the time and effort to learn this technique. The level of training and experience of the user may well determine the effectiveness of dermoscopy. A review paper recommended that dermoscopy should be used by experts to increase test accuracy ***(Massone et al., 2005).***

The time necessary to complete an examination using the technique may be considered a negative factor in its use. In one study, almost one-third of dermatologists thought that the use of dermoscopy was too time consuming ***(Noor et al., 2009).***

A complete skin examination with dermoscopy took significantly longer time compared with a complete skin examination without dermoscopy and total body photography.

However, since the total time required for a thorough complete skin examination (with or without dermoscopy) was