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ORIGINAL ARTICLE

Early diagnosis of melanoma: what is the impact of dermoscopy?

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ABSTRACT: There are three possible explanations for the improved melanoma recognition when a clinician uses dermoscopy: first, the presence of early dermoscopy signs that become visible in melanoma much before the appearance of the classical clinical features; second, an increased attitude of clinicians to check more closely clinically banal-looking lesions; and third, an improved attitude of clinicians to monitor their patients. In this review, the light and the dark sides of melanoma screening are briefly discussed, including the need to find better strategies to decrease the number of unnecessary excision of benign lesions on one hand, and to finally decrease melanoma mortality rates on the other.

KEYWORDS: dermatoscopy, dermoscopy, early diagnosis, melanoma

Introduction

Dermoscopy undoubtedly allows a better detection of melanoma, but what are the specific reasons? There are three possible explanations: first, the presence of early dermoscopy signs that become visible in melanoma much before the appearance of the classical clinical features; second, an increased attitude of clinicians to check more closely clinically banal-looking lesions; and third, an improved attitude of clinicians to monitor their patients.

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Early dermoscopy criteria

For years, the simple ABCD rule represented our clinical guideline to differentiate melanoma from benign moles and, undoubtedly, its introduction allowed a dramatic improvement in the early detection of melanoma (FIG. 1) (1). However, the ABC criteria (asymmetry in shape, border irregularity, and color variegation) become more evident when melanoma is already relatively large in size

(D > 6 mm). Clearly, melanoma is already melanoma when it is smaller than 6 mm, and shape, border, and color might be relatively regular at this stage. The advantage of dermoscopy is that equivocal features are often present in very small melanomas, thus increasing our index of suspicion even in the context of small and clinically banal-looking melanomas (FIG. 2) (2).

Complete skin examination

As a consequence, clinicians are today more prone to examine dermoscopically even small and banal-looking lesions. This is in contrast to one of the guiding rules of a few years ago, namely, dermoscopy is best suited as a second-level diagnostic tool for clinically suspicious lesions (3,4). Today, dermoscopy has to be considered as a first-level screening tool to increase the number of early excised melanomas. In contrast to the cumbersome equipment used a few years ago, dermoscopy today is performed using inexpensive and handheld instruments. Few of them are provided with a polarized light that does not require the use of the fluid to render the epidermis translucent. This translates into a much faster screening in the clinical setting.

In a recent randomized study, a group demonstrated that dermoscopy is indeed not time-consuming (5). To determine the time required to perform a complete skin examination with and without dermoscopy, 1328 patients with at least one melanocytic or non-melanocytic skin lesion were randomly selected to receive a complete skin examination with or without dermoscopy. The median time needed for complete skin examination without dermoscopy was 70 seconds and with dermoscopy was 142 seconds, a significant difference of 72 seconds ($p < 0.001$). However, a thorough skin examination, with or without dermoscopy, requires less than 3 minutes, which is a reasonable amount of time to potentially prevent the morbidity and mortality associated with skin cancer (FIGS 3 and 4).

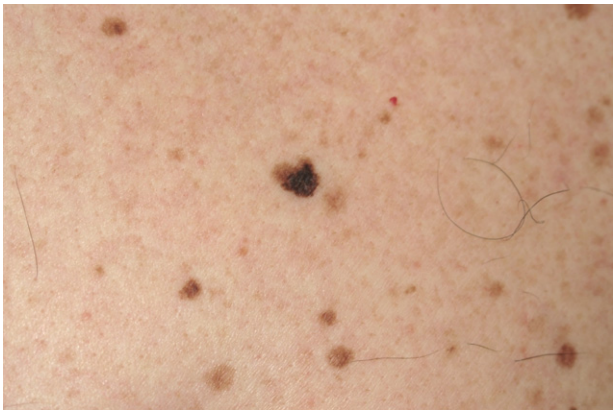

FIG. 1. Early melanoma clearly recognized by the clinical ABCD rule. Note the striking morphologic differences of the central melanoma with the small nevi around.

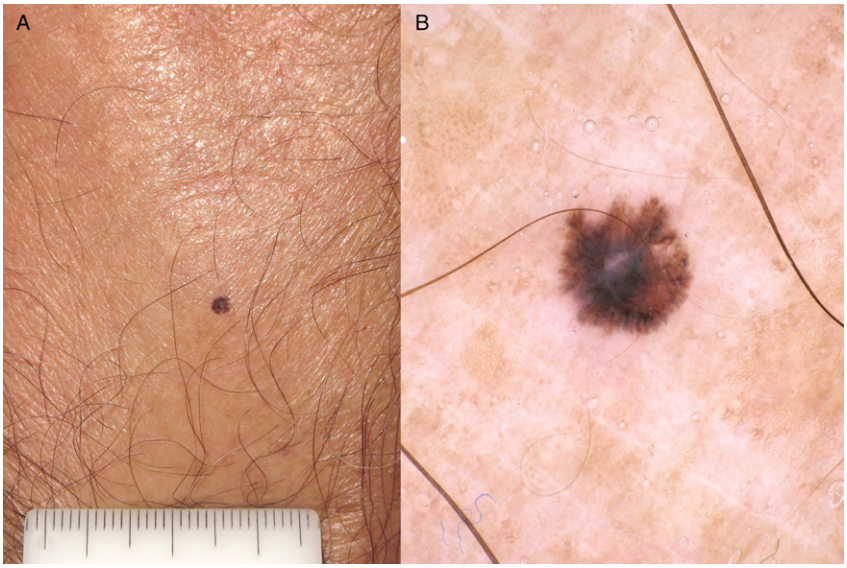

FIG. 2. Melanoma in situ on the arm of a 45-year-old man. (A) Clinically, the lesion is small and relatively regular in shape, border, and color. (B) Dermoscopically, a combination of melanoma-specific features are clearly evident, including asymmetry of color and structure, irregular streaks, and blue-white structures.

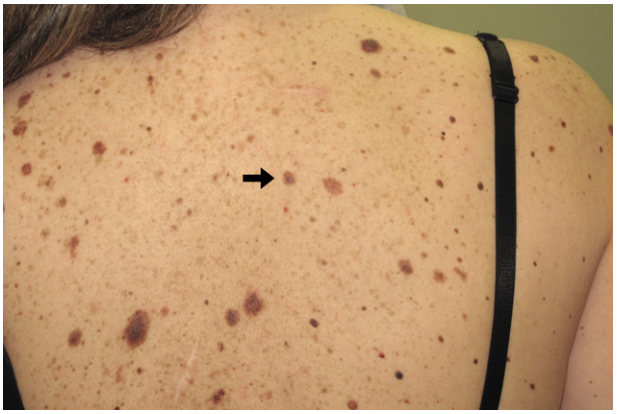

FIG. 3. With the naked-eye examination, it is very difficult to recognize the small-sized and regularly shaped melanoma (arrow) among the multiple ugly nevi present on the back of this patient.

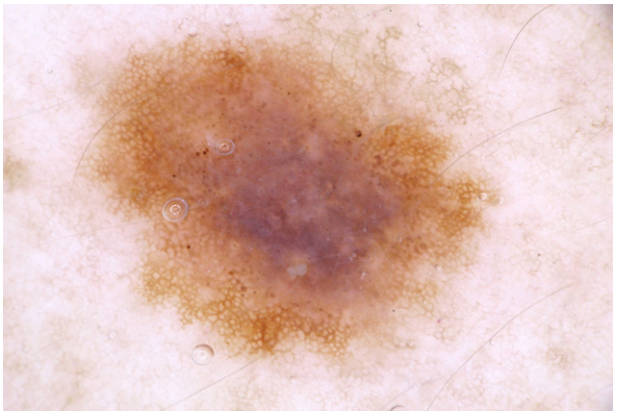

FIG. 4. Dermoscopically, the melanoma shown clinically in FIG. 3 is easy to be recognized because of the atypical network, the irregular globules, and the striking blue-white structures in the center.

Monitoring patients with multiple moles

If dermoscopy is employed as a screening tool for complete skin examination, the number of early detected melanomas increases, but there is a variable percentage of melanomas that may still be missed at the first consultation. This is because initial melanoma may be clinically but sometimes also dermoscopically indistinguishable from benign lesions, especially in the context of patients with the "ugly mole syndrome" (patients with multiple, clinically atypical melanocytic nevi, formerly called "dysplastic mole" syndrome). In the management of these patients, 2 different strategies are employed. The first consists of removing all atypical lesions, resulting in a high number of unnecessary excisions of melanocytic nevi. The second

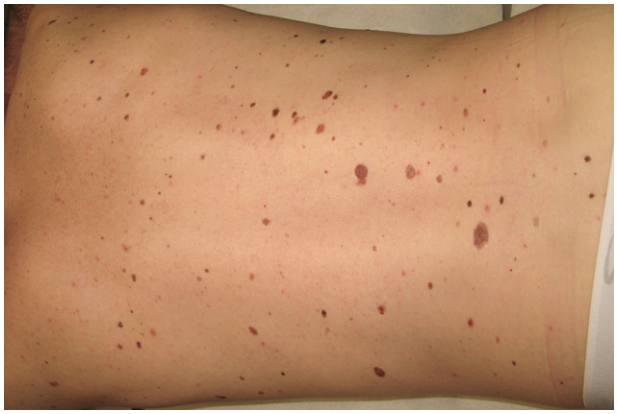

FIG. 5. A 42-year-old man with multiple nevi on the back.

strategy involves dermoscopic follow-up and excision of only those lesions that change over time. Digital dermoscopic monitoring of melanocytic lesions offers the dual advantages of increasing the likelihood that featureless melanomas are not overlooked while minimizing the excision of benign lesions (FIGS 5–7) (6–9).

The number needed to treat in the dermoscopy era

One of the most useful metrics for measuring accuracy in melanoma detection is the number needed to excise (NNE), calculated as the number of melanocytic lesions excised for every confirmed melanoma. NNE values vary according to clinician expertise, with reported values ranging from 20 to 40 for general practitioners at nonspecialized clinics, from 19 to 28 for general practitioners at skin cancer clinics, and from 4 to 18 for dermatologists at specialized clinics (10–14).

Two meta-analyses performed in both experimental and clinical settings have shown that when used by experts, dermoscopy is associated with a significant improvement of sensitivity for melanoma (15,16). In two additional studies, one randomized and one retrospective, experts using dermoscopy were able to improve the NNE value by decreasing the number of unnecessary excisions of benign lesions (12,13). However, data are lacking that might reveal whether dermoscopy could similarly improve accuracy of melanoma detection in nonspecialized clinical settings (NSCS).

The present authors conducted a multicenter survey to investigate (i) changes in NNE values over a 10-year period (from 1998 to 2007); (ii) differences in NNE values at specialized clinical setting (SCS) versus NSCS; and (iii) patient factors influencing NNE values (17). The most striking result

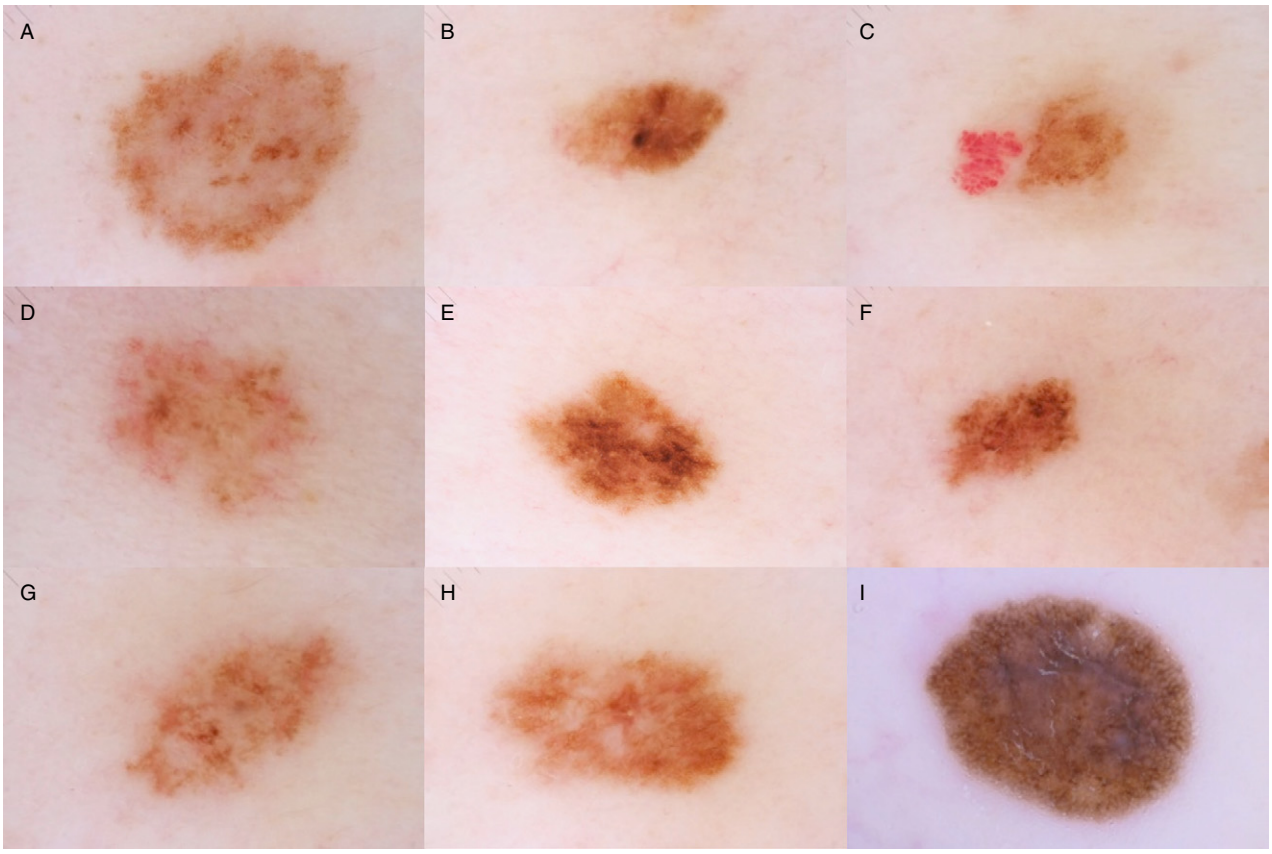

FIG. 6. **At the baseline dermoscopic examination of the patient shown in FIG. 5, lesion I was considered suspicious enough to require excision and the histopathologic examination revealed a melanocytic nevus. The rest of the lesions were monitored. All of them were proven to be stable, except lesion E, which changed asymmetrically and diagnosed as melanoma histopathologically.**

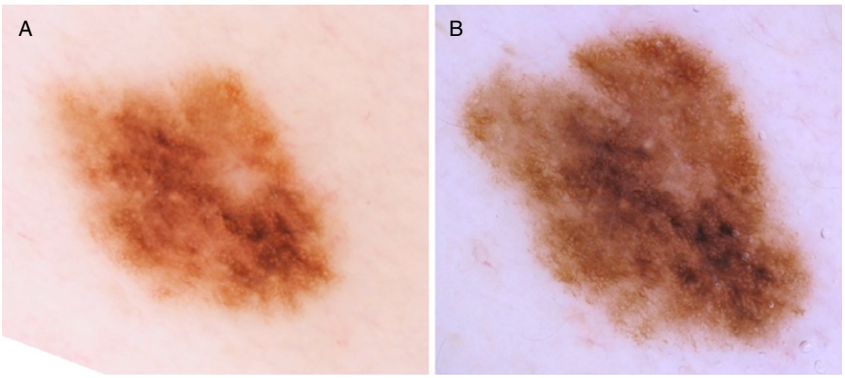

FIG. 7. **Baseline and follow-up dermoscopic image of lesion E shown in FIG. 6. After 2 years the lesion was removed because of the asymmetric growth and proven to be a melanoma in situ histopathologically.**

of the present study was the finding that the NNE decreased significantly over time in SCS, yet remained stable in NSCS. In SCS the NNE decreased from 12.8 to 6.8 in the 10-year study period, whereas it remained essentially unchanged at approximately 29 in NSCS.

Most of the effect on NNE in SCS was due to the striking increase in the number of excised melanomas and, as a consequence, to the decreasing proportion of excised nevi. The growing trend to use dermoscopy in SCS may be responsible for the improving NNE obtained in these centers from 1998 to 2007. Other than aspects related to the physician's expertise, various additional factors have a strong influence on the NNE, including those related to the lesion and to the patient. In the

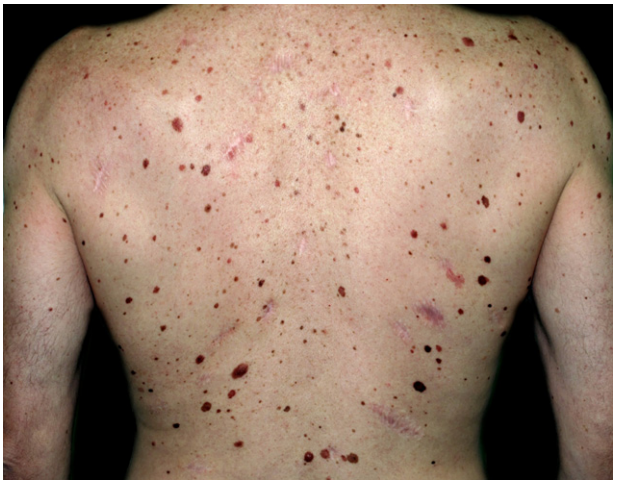

FIG. 8. A 38-year-old man with multiple nevi and multiple scars because of previous excisions of nevi. This is the prototype patient explaining why much of the economic burden of melanoma screening results from excisions and biopsies of benign lesions.

present study the authors found higher NNE rates in the youngest age group and in patients with lesions located on the trunk. Various factors may be relevant in interpreting these data. First, the likelihood of melanoma increases with increasing age and is extremely rare in anyone younger than 20 years old. Second, most of the patients with multiple nevi and the "ugly mole" syndrome are aged between 20 and 50 years. Nevi that exhibit atypical clinical features require excision to rule out melanoma; consequently, much of the economic burden of melanoma screening results from excisions and biopsies of benign lesions, especially in patients with multiple nevi (FIG. 8). Then, what could it be a reasonable strategy to minimize this problem?

The comparative approach in patients with multiple nevi

Given that clinical and dermoscopic assessments of morphologic features in individual lesions may be insufficient among patients with the "ugly mole" syndrome, a useful additional strategy might be a comparative approach in which individual lesions are evaluated in the context of a patient's overall nevus profile. This approach is based on recognition of the "signature nevus" or the "ugly duckling sign" (18–20). Most individuals have a predominant group of nevi sharing a similar clinical (or dermoscopic) appearance (the signature nevus); therefore, a lesion outside of the common nevus pattern in a given individual (the ugly duckling) must be considered with suspicion, even if it does not fulfill the ABCD or melanoma-specific dermoscopic criteria. Conversely, an atypical lesion may be completely normal in an individual whose skin is covered with similar lesions.

The present authors performed a study to assess the outcome on management recommendations of two approaches to dermoscopy. A dermoscopic morphologic approach (assessment of a single lesion) was compared with a dermoscopic comparative approach (assessment of multiple lesions) in a series of patients with the ugly mole syndrome. In our study, the comparative approach dramatically reduced the number of management recommendations favoring excision (21). In that series, only 14% of lesions were judged to merit biopsy using the comparative approach compared with 55% using the morphologic approach, when the same lesions were judged individually without consideration of a patient's other lesions. Assessing individual lesions in the context of a patient's multiple nevi to find the ugly duckling is what clinicians extensively do in their routine practice. However, the clinical outcome of this procedure, especially in the context of dermoscopy, had been not tested to date. Our study results suggested that unnecessary excisions can be reduced by the use of a comparative approach rather than a morphologic approach in dermoscopic evaluation of equivocal lesions among individuals with multiple ugly nevi (FIG. 9).

Melanoma mortality

The bad news is that melanoma mortality is not reduced, in spite of clinicians' efforts to diagnose melanoma earlier (22,23). In our view, there are three avenues to approach the task of reducing melanoma deaths: the first is to alter the tumor itself, particularly the fast-growing subtype; the second is to modify patient behavior; and the third is to concentrate on what the physician can do. On which of the three actors should efforts be concentrated on? Unfortunately, nothing can be done to change the aggressive behavior of some melanomas, and it would be very difficult to teach the whole population how to recognize fast-growing melanomas early enough to prevent growth and metastases. Thus, the only way to reduce melanoma deaths is to focus our attention on the third actor, the physician; but the challenge is not only the recognition of fast-growing melanoma once it is seen, but, indeed, to get the chance to see it! How many times has a full-body skin examination been performed when the patient is coming for hand

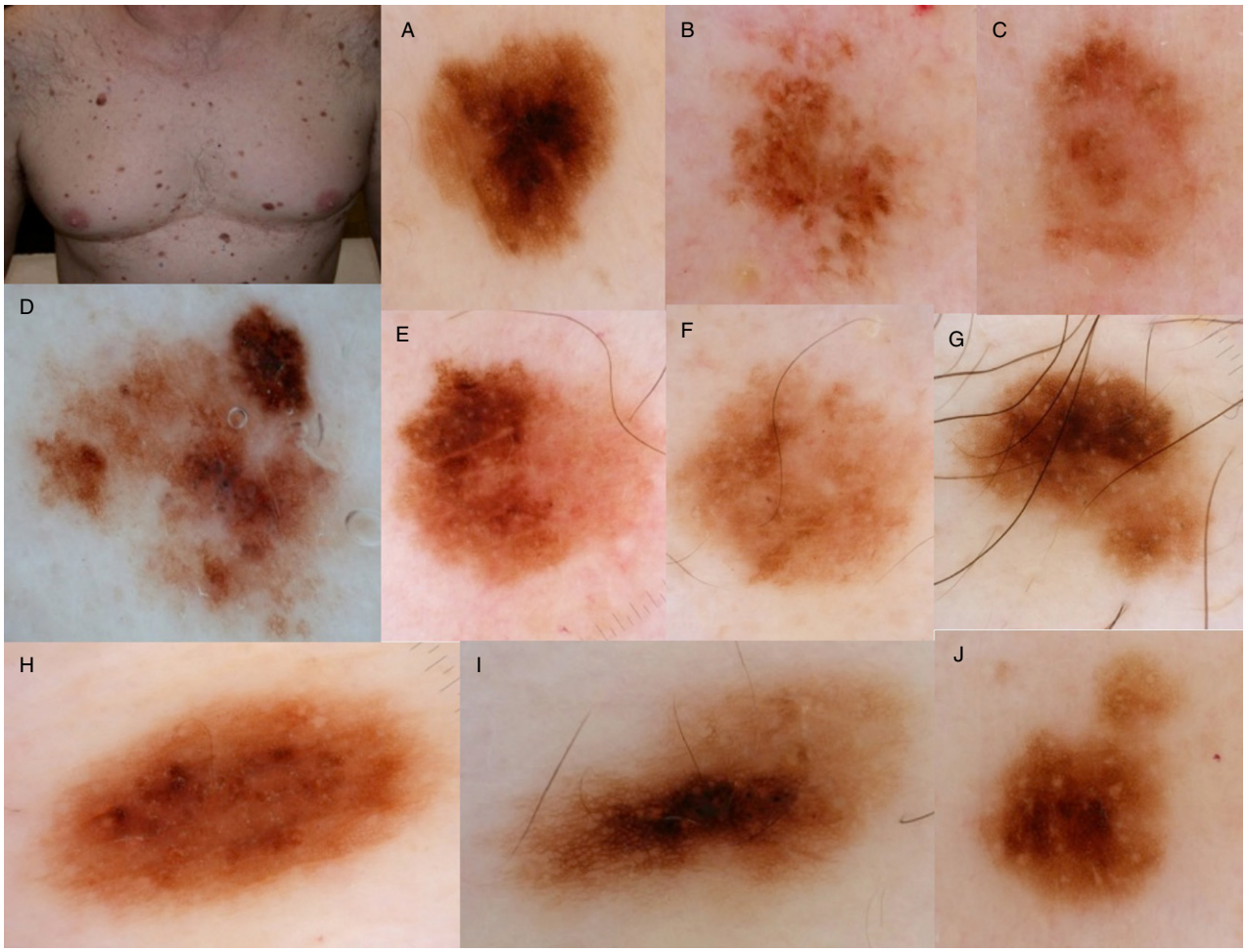

FIG. 9. **A 62-year-old man with multiple nevi. Each of them shows a variable degree of irregular features dermoscopically, but lesion D is the most suspicious one. Only this lesion was thus excised and diagnosed as melanoma histopathologically.**

dermatitis or cosmetic procedures? As dermatologists, the authors have to confess, the answer is: very rarely!

It is actually proven that although most patients with melanoma have at least one medical consultation in the year before diagnosis, only 20% report receiving a skin cancer examination (24). In a previous randomized trial, the present research group demonstrated that a group of general physicians using dermoscopy performed 25% better triage of suspicious skin tumors than physicians who used naked-eye examination alone (25). At the beginning of that study, just a short dermoscopy course (only 2 hours) was given to general physicians. Thus, the present research group speculated that the increased dedication of physicians to the patients, a sine qua non condition to perform dermoscopy, was in itself one of the main reasons for the increased detection rate of suspected skin malignancies.

In another prospective, multicenter study on patients with focused skin symptoms (who would not normally receive a routine total body skin examination (TBSE)), the present authors wanted to test the absolute and relative risks of missing skin cancer, in the absence of TBSE, and the estimated number of patients examined by TBSE for detection of at least one skin cancer (26). Our study demonstrated that TBSE for patients presenting with localized dermatologic problems allows detection of many skin malignancies that would otherwise be missed. In a population of patients who were not scheduled to undergo a complete skin examination, 47 patients need to be examined by TBSE to find one skin malignancy (including melanoma and nonmelanoma skin cancer (NMSC)), and 400 patients to find one melanoma. Factors that significantly increased the likelihood of finding a skin cancer by TBSE were: older age (especially in those patients with a history of NMSC or with fair skin type), patients consulting for a skin tumor, and patients with an equivocal lesion on uncovered areas (FIG. 10).

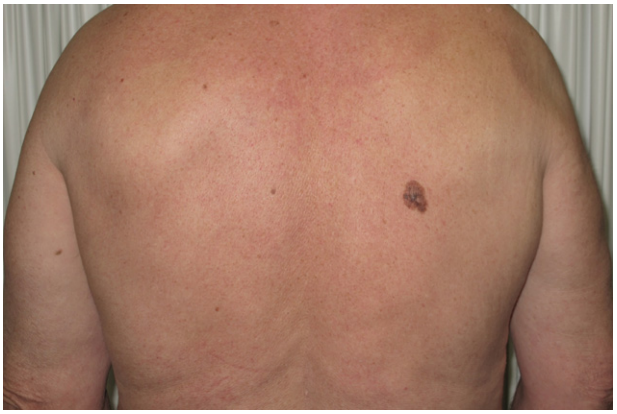

FIG. 10. A 75-year-old man with a large melanoma on his back. The clinical diagnosis is straight forward, but the lesion was not actually seen during previous medical consultations performed by the patient for his rosacea.

In conclusion, while waiting for definite results concerning the impact of skin cancer screening on mortality and morbidity, TBSE should continuously be performed to not miss melanoma and NMSC. The screening procedure is effective in detecting skin cancer, and the risk of harm from unnecessary biopsies (false-positive results) is reasonably low.

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