Early Diagnosis of Cutaneous Melanoma
Revisiting the ABCD Criteria

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The ABCD acronym for melanoma screening was devised in 1985 to provide the lay public and primary health care professionals with a useful and memorable mnemonic to aid in the early recognition of potentially curable cutaneous malignant melanoma. The now well-known parameters of Asymmetry, Border irregularity, Color variegation, and Diameter greater than 6 mm are used globally in medical education and in the lay press to provide simple parameters for appraisal of pigmented cutaneous lesions that may need to be further examined by a specialist. Specialist evaluation may result in further workup of pigmented lesions via dermatoscopy, biopsy, or both.2

Over the course of their 19-year history, the ABCD criteria have been widely described,3-5 disseminated,6-9 verified,3,4,10 and debated.11-13 We review key literature regarding the applications and utility of ABCD, revisit the D criterion in light of recent data regarding small-diameter melanomas, and consider expansion of the acronym to ABCDE, which includes a criterion for evolving (ie, lesions that have changed over time).

EVIDENCE ACQUISITION
Cochrane Library and PubMed searches for the period 1980-2004 were conducted using search terms ABCD and melanoma and small-diameter melanoma. Bibliographies of retrieved articles were also used to identify additional relevant information.

Evidence Synthesis
Available data do not support the utility of lowering the diameter criterion of ABCD from the current greater than 6 mm guideline. However, the data support expansion to ABCDE to emphasize the significance of evolving pigmented lesions in the natural history of melanoma. Physicians and patients with nevi should be attentive to changes (evolving) of size, shape, symptoms (itching, tenderness), surface (especially bleeding), and shades of color.

Conclusions The ABCD criteria for the gross inspection of pigmented skin lesions and early diagnosis of cutaneous melanoma should be expanded to ABCDE (to include “evolving”). No change to the existing diameter criterion is required at this time.

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EVIDENCE SYNTHESIS

Genesis, Validation, and Critique of the ABCDs

In 1985, members of our group devised the ABCD acronym in response to an increasing melanoma incidence with little to no public awareness. Indeed, melanoma incidence increased steadily in the United States throughout the 20th century, most recently increasing from 7.5 per 100000 in 1973 to 22.6 per 100000 in 2001 among white populations (the group at highest risk for melanoma). Despite reports of cohort-specific improvements, overall melanoma incidence and mortality continue to increase in the United States and elsewhere, making the early recognition of melanoma a continuing public health priority.

The ABCD criteria were intended as a simple tool that could be implemented in daily life, a mnemonic “as easy as ABC,” to alert both the layperson and primary care physician to the clinical features of melanoma. Based on our experience evaluating patients in the melanoma cooperative group at New York University School of Medicine, we found that asymmetry, border irregularity, and color variegation were consistently associated with lesion diameter greater than 6 mm. These observations led to the creation of the current A, B, C, and D criteria. This acronym was first described in 1985; in 1993, the research basis for ABCD was presented more thoroughly.

It should be emphasized that ulcerated lesions were excluded in the initial analysis because we sought to elucidate features of early melanoma. Pigmented skin lesions that were ulcerated without a history of antecedent trauma would have been already highly suspicious for advanced melanoma and would have required biopsy regardless of other features, justifying their exclusion from analysis. The ABCDs were thus intended to help describe a subset of melanomas, namely early, thin tumors that might otherwise be confused with benign pigmented lesions. Also, it should be emphasized that the criteria were developed to assist nondermatologists in differentiating common moles from cancer and were not meant to provide a comprehensive list of all melanoma characteristics.

A few investigators have critiqued the original ABCD criteria in principle and in practice. Grob pointed out that atypical nevi and seborrheic keratoses can share many of the ABCD properties of melanomas. Nevertheless, the ABCD criteria have been verified in 3 studies documenting their diagnostic accuracy in clinical practice. As shown in Table 1, the sensitivity and specificity of these criteria vary when used singly or in combination, and sensitivity declines as specificity increases. In addition, Barnhill et al investigated interobserver variability and reported moderate but significant agreement in most clinical features, including irregular borders and multiple colors, among 4 physician evaluators (P < .001). The combination of reliable sensitivity and specificity in addition to adequate interobserver concordance in the application of the ABCD criteria supports the ongoing utility of this screening instrument in clinical medicine. It should be emphasized that not all melanomas have all 4 ABCD features. It is the combination of features (eg, ABC, A+C, and the like) that render cutaneous lesions most suspicious for early melanoma.

Revising the D Criterion: Increasing Evidence of Small Melanomas

While the A, B, and C criteria of 1985 have been widely accepted, a growing body of literature documenting the existence of small-diameter melanomas, defined as those 6 mm or less in diameter, has prompted us to reevaluate whether the D criterion needs to be revised. We identified 6 retrospective reports quantifying the prevalence of small-diameter cutaneous melanomas in cohorts of at least 30 patients, including one by our own group. Currently, it is unclear what proportion of all melanomas are less than 6

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<th>Table 1. Summary of Key ABCD(E) Sensitivity and Specificity Studies</th>
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<td>McGovern and Litaker, 1992</td>
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<td>Healsmith et al, 1994†</td>
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Abbreviations: ABCD, Asymmetry, Border irregularity, Color variegation, Diameter greater than 6 mm; CI, confidence interval
*The authors used lesion diameter 6 mm or greater as the cutoff for this study and tested an E criterion (for horizontal enlargement).
†The authors tested E for elevation.
mm in diameter, and more importantly, what proportion of pigmented lesions 6 mm or less in diameter are melanomas. Various authors report that small melanomas include less than 1% to 38% of all invasive melanomas.

Most small-diameter melanoma studies are limited by the fact that they are retrospective reviews of pathology specimens and do not always consider the key issue of ex vivo tissue shrinkage in their analysis. A notable exception is the 1999 article by Bono et al of 270 consecutive melanoma cases, which measured melanoma diameters on relaxed skin, prior to excision. Among all small-diameter melanoma studies we reviewed, the methodology used by Bono et al most closely approximates lesion measurement techniques used in clinical practice. In their series, the authors found that 33 (14%) of 231 invasive melanomas were small-diameter lesions.

Published data regarding melanoma specimen shrinkage have important implications for the analysis of small melanoma data generated from histopathologic specimens. Silverman et al performed the largest available study of tissue shrinkage and found a mean, age-related shrinkage of 20% comparing in vivo with postfixation measurements for 407 cutaneous melanomas. Using an algorithm based on these results, we determined that lesion diameters reported in specimen-based studies as 4.8 mm or greater postexcision may well have measured 6 mm or more in vivo, before surgical removal.

Based on available data, we reanalyzed 4 studies from the literature on small-diameter melanomas using the formula of Silverman et al to estimate the actual size of pigmented lesions on patients’ skins. After adjusting for tissue shrinkage among specimens from our Australian cohort, we found that 10% of invasive melanomas were small-diameter tumors, in contrast to the 31% previously reported. The results of the other 3 studies, which included lesions mostly less than 5 mm in diameter, were little changed in our analysis. Data from these studies suggested that small-diameter melanomas represented less than 5% of all invasive melanomas. Since the literature on small-diameter melanomas does not present data on the diameter of benign pigmented skin lesions for comparison with malignant lesions, we do not know what proportion of all small-diameter (ie, ≤6 mm) lesions are melanomas, an important consideration if the D criterion is to be revised.

The outcomes of invasive small-diameter melanomas have not been well-established, as existing reports focus on only short-term patient follow-up and presented very limited long-term mortality data. Such outcomes may be best understood in a framework that considers lesion thickness in addition to lesion diameter. Tumor thickness, a measurement of tumor invasion into the dermis, is a powerful prognostic factor and a key component for the staging of localized melanoma. In published data from other groups, small-diameter melanoma tumor thicknesses ranged from 0.11 to 1.5 mm, with a median thickness of approximately 0.7 mm. Studies of melanoma outcome would predict a favorable prognosis for the majority of such relatively thin tumors.

In contrast to the short-term follow-up described above, we obtained new follow-up data, ranging from 10 to 14 years, from the Australian cohort on which we previously reported. Our focus was to extract information regarding the specific question of mortality attributed to small-diameter melanomas that could have been diagnosed based on the ABCD criteria. We included patients with nonulcerated lesions measuring 6 mm or less in diameter after adjustment for tissue shrinkage. Based on these inclusion criteria, 2 patients died from nonulcerated, small-diameter (5.8 mm and 5.9 mm) melanomas. In contrast to the published reports we reviewed, both of our patients had locally advanced, thick tumors, 2.1 mm and 3.8 mm in thickness, respectively, with mitotic indexes of 18 and 5 mitoses/mm². A mitotic index greater than 5 mitoses/mm² has been correlated with poor prognosis, independent of tumor thickness in some studies. The survival times of these patients were 52 and 14 months, respectively. No other published studies reported patient deaths, although Kamin et al reported 1 recurrence and 1 metastasis after median follow-up of 16 months. Despite the lack of clarity regarding the proportion and clinical course of small-diameter melanomas relative to all melanomas, it appears that invasive melanomas 6 mm or less in diameter are uncommon and such lesions infrequently cause metastatic disease since they are generally removed at early stages of tumor progression.

Revision of the D criterion depends less on the proportion of small-diameter melanomas among all melanomas than on the frequency of small melanomas (≤6 mm in diameter) among the universe of all pigmented cutaneous lesions of similar diameters. This frequency would be difficult to calculate as the vast majority of pigmented lesions 6 mm or less are obviously benign and thus are not biopsied. Overall, it has been estimated that among pigmented cutaneous lesions there are 90,000 benign nevi to every 1 melanoma.

Based on the above considerations, we do not believe that lowering the diameter criterion of the ABCD framework will increase sensitivity of melanoma diagnosis without seriously compromising specificity and generating millions of unnecessary skin biopsies. Costs, scarring from surgical procedures, and patient anxiety must be considered in the estimation of public health implications associated with lowering of the D criterion. The ABCDs have the greatest diagnostic accuracy when used in combination, a concept that should be kept in mind when evaluating pigmented lesions 6 mm or less in diameter. When such small lesions have only 1 of the other ABC criteria, follow-up observation of its evolution, if present, can lead to the eventual, early diagnosis of cutaneous melanoma.

The Case for an E Criterion

The ABCD acronym was originally designed to provide the lay public and physicians with easily memorable criteria to
recognize the extant physical characteristics of early melanomas. Since their description nearly 20 years ago, evidence has accumulated that the addition of “E” for “Evolving” will substantially improve and enhance the ability of physicians and laypersons to recognize melanomas at earlier stages. “E” for Evolving recognizes the dynamic nature of this skin malignancy. This is especially important for the diagnosis of nodular melanomas, which frequently present at more advanced stages (ie, thicker tumors), thus contributing greatly to melanoma mortality rates.19,33,34

Nodular melanomas frequently lack asymmetry, border irregularity, color variegation, and diameter greater than 6 mm.20,35 However, in one series of 125 patients, lesion change (ie, evolution) was noted in 78% of nodular melanomas.20 Among the 92 patients with the more common superficial spreading melanoma, 71% noted evolution of their lesion.20 These data are consistent with previous data from our group in which 615 (88%) of 696 patients noted evolution in their melanoma prior to its removal.33

We support expansion of the ABCD criteria to include an E for evolving (ie, lesion change over time) (FIGURE). We define “evolving lesions” as those noted to have changed with respect to size, shape, symptoms (eg, itching, tenderness), surface (eg, bleeding), or shades of color. Others have proposed various “E’s” to be added to ABCD. We prefer the term “evolving” to “enlargement”4 because enlargement focuses on the size of a lesion alone and excludes consideration of color changes, which are part of the evolution of many melanomas. E for “elevation”36 would be misleading because significant elevation is not apparent in most early melanomas and is thus not a warning of early disease.5,26 “Evolving” is a simpler term than “evolutionary change”13,37 and could be more readily incorporated into public educational materials. The term “evolving” subsumes the concepts of change, enlargement, and elevation.

The importance of lesion evolution as a cardinal feature of cutaneous melanoma, and a frequent cause of excision among lesions ultimately diagnosed as melanoma, is well supported.4,25,30,32,38,39 Although patient report has been criticized for its subjectivity in comparison with more objective assessments of asymmetry, border, and color,17 a 2001 review by Grichnik of “difficult early melanomas” supports the importance of soliciting patients’ history of lesion changes in differentiating melanoma from atypical nevi.32 A study by Cassileth et al of presenting symptoms in malignant melanoma found that changes in “size, elevation and color” were the most frequent cluster of symptoms reported by patients as catalysts precipitating medical evaluation.38 Other symptoms noted to be significant were bleeding, itching, tenderness, elevation, and ulceration.38

Three studies lend additional support to the importance of lesion evolu-
tion in the diagnosis of cutaneous melanoma. Based on their calculation of the sensitivities and specificities of each of 5 ABCDE criteria (using E for horizontal enlargement, which is a feature of an evolving lesion), Thomas et al concluded that enlargement is the most specific criterion among the ABCD(E)s (Table 1). Lucas et al, in a study of dermoscopic features of 169 pigmented lesions, found that lesions noted by dermatologists to be both nonuniform (ie, sharing some of the ABC criteria) and changing had at least a 4 times greater chance of being melanoma than lesions that did not meet these characteristics. The study by Healsmith et al of the sensitivity of the ABCD(E) criteria in diagnosing 65 melanomas revealed that all 5 lesions missed by the ABCDEs (with E for elevation) had been noted by the patient to have evolved (ie, changed in size over time).3

The concept of lesion evolution has a prominent place in the Glasgow 7-point checklist, which highlights changes in size, shape, and color as major signs of melanoma. As demonstrated in Table 2, the addition of E (for evolving) adds these major criteria to the ABCDs. These criteria are based in part on the observation that 89% to 95% of 100 consecutively accrued melanomas demonstrated changes in these features, and 100% showed change in at least 1 feature. Minor criteria in the checklist include sensory change, diameter of 7 mm or greater, and the presence of inflammation, crusting, or bleeding, as these were observed less frequently. Perhaps due to its greater complexity, however, the Glasgow checklist has been less widely adopted than the ABCD criteria.

Expansion to ABCDE will broaden the education of physicians and the lay public in the clinically significant historical features of pigmented cutaneous lesions, especially the evolving nature of early melanomas. Evidence suggests this may improve the early diagnosis of melanoma. In 2001, Harris et al published an Internet-based study of skin cancer education. This included modules on the recognition of melanoma using an algorithm that combines the ABCD criteria with the importance of a changing lesion, included in the Glasgow 7-point checklist. The study population consisted of 354 physicians, 346 (92%) of whom were nondermatologists. The authors reported that a statistically significant increase in the proper management of pigmented lesions was observed. Specificity in the diagnosis of pigmented lesions increased from 69% to 89% (P<.001), with a small decrease in sensitivity, 95% to 91% (P<.001). The authors’ comment that a single case of a small melanoma that developed a change in color and was not biopsied by many participants accounted for the decrease in sensitivity. Describing this finding they state, “This information allows us to improve our program by reemphasizing the need to consider ‘change’ as well as the static characteristics of a lesion.”

Data from a population-based study in Connecticut demonstrated that increased patient awareness of melanoma signs and symptoms was significantly associated with decreased time to seek medical attention and decreased tumor thickness. The results of a public education program in western Scotland demonstrated a decrease in the diagnosis of melanomas greater than 3.5 mm thick (34% to 15%) with a simultaneous increase in the diagnosis of thinner melanomas, defined as less than 1.5 mm thick (38% to 62%). It was speculated that this shift in diagnoses to early stage disease could result in lower health care costs, as the management of thinner lesions is less costly than that of thicker lesions. The importance of public education in the clinically significant features of pigmented cutaneous lesions is also underscored by data from a 1992 population-based survey of incident cases of melanoma in Massachusetts that reported only 26% of all melanomas are identified by medical service clinicians; the remainder were diagnosed by patients themselves (53%) or by their family members (17%).

**CONCLUSIONS**

The ABCD criteria for the assessment of pigmented cutaneous lesions have been a useful screening tool in the diagnosis of melanoma, supported by evidence of reasonable sensitivity and specificity for melanoma diagnosis. While current literature reports the existence of invasive “small-diameter melanomas,” these lesions appear to be uncommon. We support preservation of the original greater than 6 mm D criterion.

In contrast, our review of the literature has led us to endorse the inclusion of “E” for “evolving,” emphasizing change over time as an important additional criterion in differentiating melanoma from benign pigmented lesions. Although not all changes in moles denote the presence of melanoma, lesions that have changed warrant further examination and possible biopsy. Future educational programs and literature about melanoma should emphasize the importance of a history of change (ie, evolving) in the assessment of pigmented cutaneous lesions. Organizations including the American Cancer Society and Skin Cancer Foundation have promoted lesion change in their educational materials; however, this feature has been described in paragraphs of text, without adequate emphasis. By adding “E” for “evolving” to the well-known ABCDs, we are stressing the importance of “E” in a more simplified message than is currently available. We believe that ABCDE is a simple, succinct, and memorable tool to educate the public, and the nondermatology and dermatology medical community about the key features of melanoma, especially lesion change.

We urge broad physician and public education in the use of the ABCDE criteria, as evidence suggests that even...
one-time instruction in the proper management of pigmented cutaneous lesions can result in immediate improvement in the capacity of clinicians and laypersons to identify cutaneous melanomas.2,46 We believe that such education will enhance the timely diagnosis of cutaneous melanoma, resulting in the surgical removal of such cancers when they are still curable.

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