EDITORSIAL

Skin Self-Examination and Melanoma

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In this issue of the Journal, Berwick et al. (1) report the findings of a case–control study in which they estimate that subjects who perform skin self-examination (SSE) have a significantly reduced incidence of melanoma and a lower risk of progression to advanced disease or death after diagnosis. If correct, this study suggests that a major reduction in melanoma incidence and mortality could be produced by a relatively simple procedure.

The most remarkable finding is the reduction in total melanoma incidence. It would be expected that self-examination, if it were an efficient method of detecting progressing melanomas early, would lead to the diagnosis of chronologically earlier and pathologically thinner melanomas without producing any change in total incidence. Indeed, the major concern about routine skin examination is that it could produce an increase in the diagnosis of thin lesions that, while clinically and pathologically classified as melanoma according to current knowledge, may not be biologically progressive (2,3). The only logical way in which SSE could reduce the total incidence of diagnosed melanoma is by the identification and removal of precursor lesions. In the Lawrence Livermore National Laboratory experience (4,5), increased awareness and surveillance resulted in a substantial increase both in skin biopsies and in melanoma incidence, although there may have been a reduction in deaths.

Thus, the reduction in melanoma incidence should be restricted to subjects in whom SSE has been followed by the removal of a precursor lesion. In the study by Berwick et al., there was a greater frequency of previous skin biopsies among those practicing SSE, which is to be expected, since previous skin biopsies are likely to be an indicator of underlying melanoma risk and a major stimulus to the performance of SSE. However, no information is given on the performance of biopsies after SSE but before diagnosis of the invasive melanoma. The demonstration of this logical process is important because, otherwise, it is impossible to exclude with confidence potential noncausal explanations for the results.

An association between the recorded performance of SSE and lower melanoma incidence could also be produced by information bias, selection bias, confounding, or chance variation. SSE is obviously difficult to assess, since it has to be assessed from the subject’s own recollection. Berwick et al. have appropriately used focus group techniques to produce a useful definition of SSE, and they have used the usual methods to protect against information bias on the part of the interviewers. However, in a retrospective study comparing patients who know they have been diagnosed with melanoma with unaffected control subjects, the possibility of subject-based information bias cannot be readily dismissed. A logical dose–response association was not seen; the degree of protection was greater in those showing casual awareness of the skin than in those using purposeful SSE, and it was least effective with those using rigorous examination methods. This pattern could reflect only random variation, but it seems inconsistent with a direct effect. The authors also collected information on physician skin examination; a comparison of the subjects’ recollection of this information with information from medical records could be reassuring.

In the study by Berwick et al., the melanoma cases represent a reasonable proportion (75%) of incident cases in a defined population. But the potential for selection bias among the controls is more of a problem. The noted response frequency of 70% represents only the frequency of response from individuals who identified themselves as eligible during a telephone inquiry following random-digit dialing. Since it is likely that some subjects will deny their eligibility as a simple method of expressing an unwillingness to participate, and since random-digit dialing is unlikely to identify all eligible subjects at the residences approached, the actual response proportion may be considerably lower than 70%. It is quite conceivable that a willingness to participate in a health survey is positively associated with a willingness to perform SSE. If the responding control subjects use SSE more than the general population from which they are drawn, an apparent protective effect will be produced. Adjustment for demographic and other variables will not necessarily control for this selection bias. However, although a bias in this direction has been shown (6), the bias demonstrated was quite small. Confounding can be severe in a study looking at a self-initiated preventive behavior. Berwick et al. have appropriately adjusted for demographic factors that could be related to health promotion behaviors, but associations with subtle factors related to the performance of such behaviors cannot be readily dismissed.

Thus, we still have to consider whether selection and information bias, or residual confounding, is as plausible an explanation of the association as is a protective effect conferred by SSE...

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(in the absence of a logical demonstration of the mechanism by which SSE has conferred that protection). Analyses by the depth of melanoma would be helpful. We would expect SSE to produce a shift toward thinner melanomas and to show the maximum protective effect with regard to thick melanomas. This finding would be consistent with the possibility that SSE has produced an increased diagnosis rate of in situ melanomas or other preinvasive lesions. In the study by Berwick et al., there was no significant association of lesion depth with SSE for all melanomas, although melanomas occurring on the back were thinner in those practicing rigorous SSE.

To assess the effect of SSE on subsequent outcome, Berwick et al. identified subjects who had either died of melanoma or had developed distant metastases, with a mean follow-up of 5.4 years. Such an analysis is open to lead-time bias, which is helpfully discussed in the article. The results showed similar rates of failure (death or distant metastases) during the first 2-3 years from diagnosis for those who practiced SSE and those who did not, with no further lethal events being recorded for the SSE group after that time. The difference in outcome frequencies is not significant. As the authors state, "additional follow-up is necessary to confirm these trends," and indeed a plateau in mortality from melanoma does not usually occur as early as 5 years from diagnosis (7).

Thus, whereas this is an interesting and innovative study, selection bias, information bias, and confounding all remain as plausible explanations for the rather remarkable association between SSE and a reduced total incidence of melanoma. The much more plausible association between SSE and improved survival after diagnosis is limited by the relatively short follow-up and the likelihood of lead-time bias, as well as the other biases. Although the authors give attention to some of these points in their article, they conclude that "SSE might reduce mortality from melanoma by 63%." Given the methodological limitations, this conclusion should be regarded as only speculative, but I suspect it will be widely quoted and used with more assurance than is warranted.

Screening for skin cancer, whether by self-examination or by examination by physicians, is already a very controversial subject. Many groups such as the American Academy of Dermatology and the American Cancer Society recommend its use without substantial qualification (8,9). In contrast, groups that rely on rigorous empirical evidence, such as the U.S. Preventive Services Task Force (10), the Canadian Task Force (11), and the International Union Against Cancer (12) have concluded that there is no rigorous evidence to support the value of skin screening. The National Cancer Institute State of the Art statement on skin cancer screening (13) is unusual in that it is supportive, but it is based only on grade 4 or 5 evidence (the two weakest levels in a five-level rating system). There are substantial potential hazards in terms of requirements for biopsies and interventions that may be unnecessary. In recent years, the incidence of lesions removed and recorded as thin melanomas has increased dramatically in many countries (3), and the pressure on physicians to remove large numbers of skin lesions is increasing. As with many other screening techniques for chronic diseases, the failure to set up an appropriate randomized trial to evaluate both the benefits and harms of the technique may well lead either to the unnecessary use of an ineffective measure or to the failure to adopt and promote an effective measure optimally. Either outcome could result in financial costs that outweigh the cost of an appropriate clinical trial. Although the widespread advocacy of skin screening in the United States may make a randomized trial particularly difficult, opportunities to conduct such a trial in other countries should still be pursued. Other study designs, such as those comparing the total experience of melanoma incidence and survival in communities that differ in terms of their extent of practicing skin examinations, could be helpful, as they were some years ago with uterine cervical cancer screening (14). The case–control study is the other major method by which skin cancer screening can be approached, and despite reservations about the conclusion, Berwick and her colleagues should be congratulated for performing the first major case–control study of this difficult topic. It is particularly difficult to define and document SSE, which makes a case–control study of this topic even more challenging than those of, for example, mammographic screening for breast cancer or sigmoidoscopy for colon cancer. It is the ability in those studies to define clearly the use of the screening technique and the precise date at which it was used that deals with some of the many methodological issues of case–control studies (15). Even in those situations, the validity of the case–control method to assess screening effects is controversial, and many authorities believe that the biases are too major to be adequately dealt with by current analytic methods (16).

The study by Berwick et al. is important, and it gives a result that should further stimulate good research on this important topic. However, uncritical acceptance of the overall conclusion is not warranted, since the alternative noncausal interpretations for the results cannot be excluded with confidence. A powerful, further analysis would be to test whether the reduction in melanoma incidence following SSE is restricted to subjects whose SSE led to the removal of suspicious skin lesions. In those individuals with no such intervention, melanoma incidence should not be affected by SSE, and a demonstration of this outcome would show the success of the control for other potential biases in the study. That, in turn, would give more confidence in interpreting the most important result, the reduction in advanced melanoma associated with the practice of SSE.

References


A videotape, Finding Strength: A Look at the Pediatric Branch, is available to health care professionals and families interested in learning more about programs and research protocols at the Branch. Also available are two videotapes for health care professionals working with HIV-infected children and their families: Conducting an HIV Parent Support Group and I Need a Friend: Kids Talk About the AIDS Virus.

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