Problems in Notification and Screening of Workers at High Risk of Disease

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Current and former workers who have been occupationally exposed to hazardous substances have unique medical and social needs. Few programs recognize and accommodate the needs of these workers. Consequently, screening and medical surveillance assume a pivotal role in a system that inadequately deals with the needs of workers identified and notified of occupational disease risks. In some cases, screening programs, ineffective in altering survival patterns, are established because they represent surrogates for other kinds of support programs that do not exist. Where screening techniques are effective and available, there still are problems in getting them funded and established in acceptable programs. This paper details these problems and argues for increased research to enhance the efficacy of screening, not only in preventing disease, but also in improving the quality of life for workers at risk.

The notification of workers at high risk of disease, particularly cancer, triggers the need for various biomedical and sociolegal services, not the least of which may be disease screening or medical surveillance.[1] Workers may be determined to be at increased risk of disease on the basis of epidemiological studies or industrial hygiene surveys. Notification is the act of informing the workers when the findings of those studies are positive. This communication is a right of study subjects and a duty of investigators. The ethical basis for this belief has been previously discussed.[1]

This paper addresses some of the problems of notification and the subsequent screening and surveillance efforts that result. Much of the information on the problems of notification and screening of workers at high risk of disease is derived from three pilot studies, reported in the literature and elsewhere in this conference.[1–4] The primary study discussed here involved the notification of a cohort of workers in Augusta, Georgia, of their risk of bladder cancer due to exposure to aromatic amines, particularly β-naphthylamine.[2]

Determination of risk usually occurs by means of epidemiological studies, but may also occur by evaluating the potential for exposure to known or suspected toxic substances. Two categories of workers "at risk" may be discerned prior to notification. One is the group of workers undergoing the exposure at the time of the risk assessment. These workers can benefit from such primary prevention as engineering controls, substitution of the hazardous agent, personal protective equipment, education, refined work practices, and medical and biological monitoring for metabolites of toxic substances. The other category presents a less ideal situation. It includes former workers or current workers whose exposures occurred in the past and who will not benefit from most of the primary preventive efforts (as far as their risk from a past exposure is concerned). Their needs, however, are manifold. Clearly this dichotomy of "at risk" workers is somewhat artificial because the groups are not mutually exclusive; some workers with past exposures and risks are still being exposed or are exposed to other carcinogens or toxins. The focus of this paper is generally on the group with previous exposures.

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These concepts are not a statement of the policy of the National Institute for Occupational Safety and Health, but are rather a presentation of the author's views as a starting point to begin dialogue on the issues.

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Screening of High-Risk Workers

Based on the National Occupational Hazard Survey conducted by the National Institute for Occupational Safety and Health (NIOSH) in 1972, it is estimated that 21,000,000 workers are now being or have been exposed to federally regulated substances (Table 1).[5] Many of these workers are at risk of disease, and some proportion are unaware of their risk. An effort is under way to develop notification programs for a few groups who are at high risk.

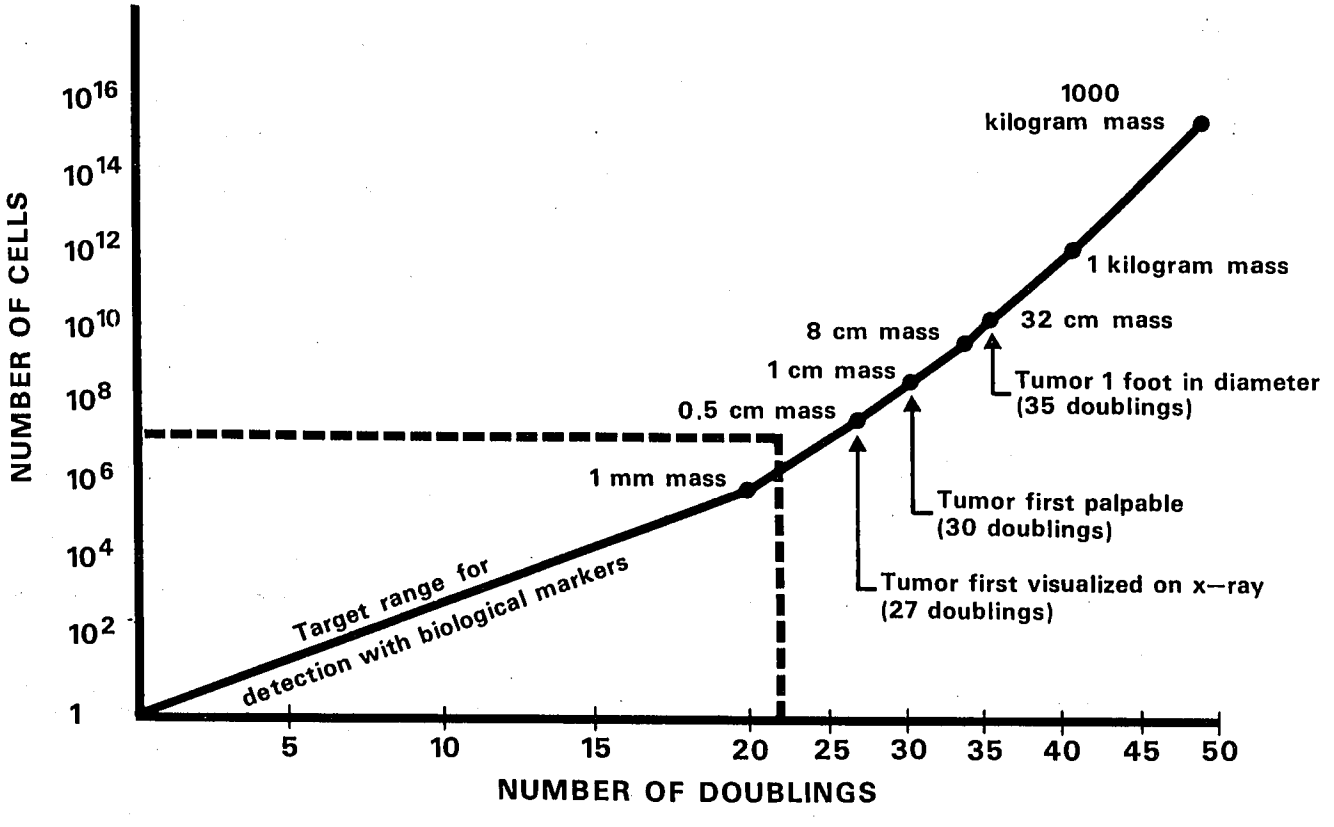
TABLE 1
Estimated Numbers of Workers Exposed to Carcinogens and OSHA-Regulated Substances*

Type of Workers	Estimated Numbers
Workers in NIOSH studies potentially requiring notification	101,000
Workers currently exposed full time to OSHA-regulated carcinogens	44,000
Workers currently exposed full time to all OSHA-rgulated substances	1,050,000
Workers currently exposed full time or part time to OSHA-regulated carcinogens	880,000
Workes currently exposed full time or part time to all OSHA-regulated substances	21,000,000

* Abbreviations used are: NIOSH, National Institute for Occupational Safety and Health; OSHA, Occupational Safety and Health Administration.

Notification triggers a process that involves a need for services that, among other things, is tied to screening and medical surveillance. The rationale for this is clear: once workers are told of a risk, they usually want to do something about it. Most likely, they seek medical attention, but they also seek a climate of support. Unfortunately, with regard to cancers, few means of early disease detection are available that improve the survival of persons any better than if they are not treated until they have symptoms (provided they recognize the early symptoms).[6,7] This statement implies that screening is inadequate; however, in some cases, the problem may be that therapeutic limitations prevent taking advantage of the early detection of disease.

Our clinical colleagues may argue that there is no biological or clinical difference between tumors detected early and those found at the time of symptomatic presentation. In some cases, this may be true. The oncologist rarely has the opportunity to diagnose or treat a disease "early," and it is important to realize how "late" the disease is diagnosed.[8] This is graphically demonstrated in Fig. 1. A 5-mm tumor already has undergone approximately 27 doublings and may contain 10^8 maligmant cells. A bladder tumor, during its preclinical stages of evolution, has survived about 80% of its natural temporal history prior to causing symptoms leading to its diagnosis.[9] What we call "early detection" is really very late in the process. However, this situation is not static. Aggressive research in both detection technologies and



(Adapted from Anderson, 1979)

Fig. 1. Relationships of tumor size, cell number, and tumor doublings.[8]

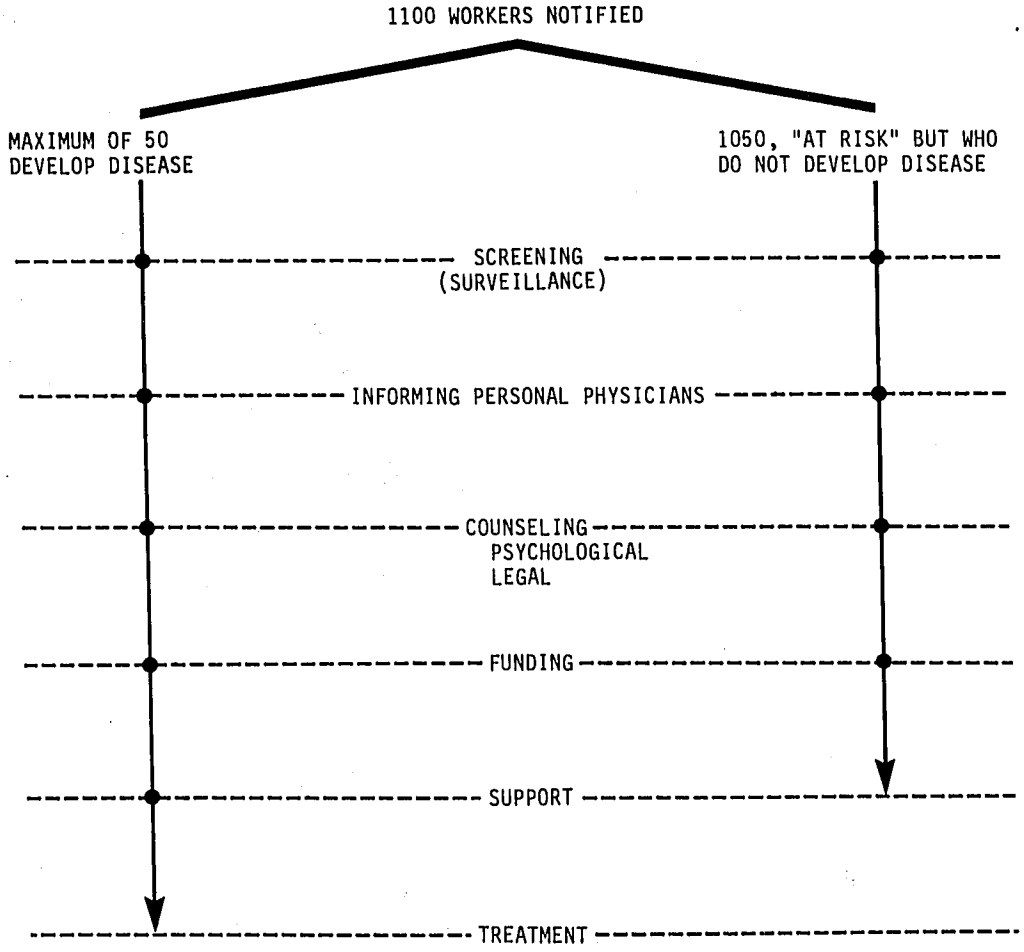


Fig. 2. Comparison of the needs of potential cases and noncases among workers notified of their risk of bladder cancer.

disease therapies could result in the ability to detect and treat disease earlier and consequently more effectively.

The screening debate, couched in terms of survival, probably represents a narrow view of the picture. The whole process of persons' lives must be viewed, from the time they are found to be at risk for a disease, through the time when the disease is detected, to the time they die, whether from the disease in question or from another cause. A determination should then be made if the course and quality of those lives are altered by that detection. This is difficult, and it raises such questions as, "Does the lead-time effect, which results in persons knowing of their disease (cancer) earlier, balance the sum of the medical treatments that they will receive, even if the treatments are more likely to be on localized disease rather than on regional or metastasized disease?" This question has not been analyzed, and its difficulty leads one to fall back on comparisons of survival time.

The use of survival-related indicators to evaluate the effectiveness of screening programs is important for a critical appraisal but is of limited usefulness in terms of the overall needs of groups at risk. These groups, numerically at least, have more need for determining who does not have the disease than who does. This is illustrated in the following example (Fig. 2). In the Augusta study, 1,100 workers (using round numbers) were notified.[2] A maximum of 50 workers were likely to develop bladder cancer, but the 1,050 who did not would still need the same services as the cases, except for services involving treatment-related needs. A screening program for the majority of these people is an affirmation that they are still well. Such screening programs may also have a placebo-type effect. Screening usually emphasizes the detection of disease rather than the affirmation of no disease. The concepts of sensitivity, positive predictive value, lead-time biases, selection biases, and length biases are all characteristics of cases. Only specificity and negative predictive value characterize noncases, although other aspects of noncases need attention. Is the test a burden, financially or psychologically, to the worker? Do a few repeated negative tests cause the person to think that the risk is no longer present? Do they drop out of the screening program? Do family members apply the same connotation to all health risk information? In evaluating the effectiveness of a screening program for both cases and noncases, "survival" is not the only criterion that needs to be considered.

Once a cohort is identified and notified, the general

cry for screening and surveillance is understandable. Workers notified of risks, often years after the exposure, are not usually prepared for that information. Unfortunately, screening programs have often been established because they manifest concern for the plight of those at risk. Notified workers need such shows of concern and various support services. Concern and services have often been lacking due to ignorance, uncertainty, and controversial issues involving litigation. In their place, a screening program is often established. Perhaps the development of support programs should be emphasized and screening deemphasized, where the latter has been shown to be ineffective.

Instead of establishing ineffective screening programs to detect early asymptomatic disease, it might be better to focus on surveillance and education programs to ensure that workers receive prompt attention when symptoms appear. To this end, one function of notification is to ensure that workers' personal physicians are informed of the occupational risk factors that might influence the workers' health. In the Augusta study, 900 physicians in the region were informed about aromatic amine-induced bladder cancer so they could respond to specific questions.

Much of a notification effort depends on the quality and availability of information. The initial risk information may not be of the highest quality. Workers, classified as exposed on the basis of personnel records, probably represent less than the total number actually exposed, because personnel classifications fail to account for workers with specific job titles or department assignments working elsewhere in the plant. In the Augusta study, prior to notification, 66 workers were identified in the group believed, from personnel records, to be exposed (Table 2). After the participants were notified and screened, including the taking of an occupational history, 206 workers were identified as being exposed. If this cohort had been notified on the basis of a priori designations of exposure, 62% of the cases and 69% of the suspicious cases would not have received notification.[8] Conversely, it is important to have accurate risk information to preclude false notifications. However, it will never be possible to achieve complete certainty with regard to risk identification. Notifications should merely be based on a "best effort" to obtain accurate risk information.

Based on these findings, it is important to realize that the initial notification needs to be considered as one stage in a multistage process, and that the information gained from screening should be used to update cohort surveillance recommendations and for cohort management. The data from such screening programs need to be analyzed epidemiologically and the results used to make recommendations for future screenings for that cohort and others.

TABLE 2
Exposure Categorization Before and After Screening

	Before Screening		
	Exposed	Nonexposed	Total
After screening			
Exposed	50	156	206
Nonexposed	16	134	150
Total	66	290	356

$P < .001$ for McNemar's χ^2 statistic.

Another problem in the notification and screening of high-risk cohorts is the geographic dispersion of the cohort. The Augusta cohort was dispersed over 30 states.[3] The screening for those workers outside the Augusta area involved the administration of the two-part standardized protocol. A NIOSH survey specialist contacted these workers and obtained an occupational and risk factor history. Subsequently, a consulting urologist identified urologists in areas near the workers' place of residence, contacted the urologists, and engaged cooperation. The workers were then referred to the local urologists. This approach, although personal and effective in maintaining short-term continuity, is costly and time-consuming and does not allow for self-supporting, ongoing care. Such care could be maintained using this structure if the employer of the affected workers contributed funds. However, a more comprehensive approach appears to be necessary.

Biological Markers

Screening and surveillance programs are not only useful for detecting disease in asymptomatic populations, they are also useful in monitoring intervention programs such as behavioral modification and chemoprevention. For this purpose, screening is used to identify not only disease, but to look for preclinical markers whose frequency may be altered by chemoprevention and/or behavioral modifications that will subsequently result in impeding the rate of the multiple transformations necessary for cancer. The feasibility of such an approach is, in part, based on the theory that carcinogenesis is a multistage phenomenon. There are striking implications for prevention of cancer, if a multistage theory of carcinogenesis is correct. In diseases such as lung cancer due to arsenic exposure and cigarette smoking, this has been demonstrated.[10] Arsenic is an early-stage carcinogen that may not cause transformation, or will do so at a slower rate than when coupled with a late-stage carcinogenic activity such as cigarette smoking. Thus, the reduction of exposure to a late-stage carcinogen appears to be a way to alter the risk status of already-exposed workers. (This should not be interpreted as reason to be less vigilant about exposures to early-stage carcinogens.) A goal of screening research is to be able to detect cancer or precancerous stages earlier during the interval between exposure and clinical onset. The greatest technical problem in screening for cancer appears to be the inability to identify stages of the cancer process when intervention is likely to be effective.

Various biological markers hold promise as earlier indicators of occupational exposure or disease in high-risk groups.[11-16] The progress of research in this area has been rapid, and it is time to test and apply some of these recent findings. There is, however, a need to develop a strategy for biomonitoring research in high-

risk groups. Biochemistry, immunology, and genetic research have advanced so that presently many biological markers are candidates to represent human disease end points, the apparent phases of the preclinical or premalignant disease processes, or exposure. Many markers, however, are probably merely spurious correlates of the disease process and not associated with it. The problem with the good candidate markers is that their validity in human populations has not been assessed.

High-risk groups, designated on the basis of exposure studies or epidemiological investigations, offer the opportunity to validate these markers. Clearly, it is not a simple matter. Certain ethical and scientific concerns need to be addressed.

On the ethical side is the concern that the identification of unvalidated markers in human groups leaves workers without a definitive interpretation of results. On the scientific side, no criteria are available for evaluating potential techniques for their readiness for testing, nor for determining what study designs are appropriate, given the need to relate markers to disease outcomes.

Figure 3 shows a proposed strategy for research on biomonitoring techniques in high-risk groups. Biomarkers can indicate exposure, effect, or, in some cases, both.

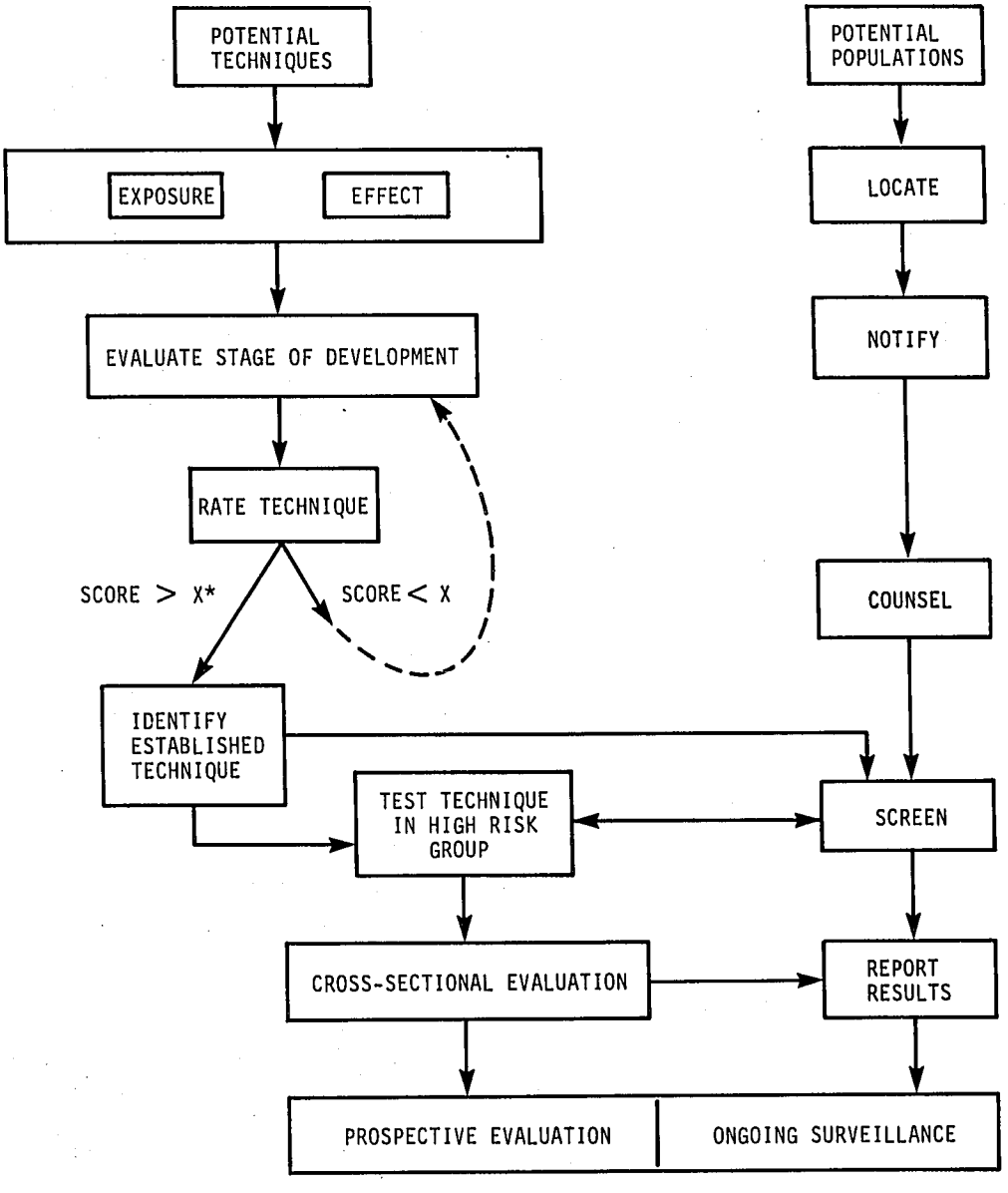


Fig. 3. Strategy for biomonitoring research in high-risk groups.

The first decision involves evaluating both the technical stage of development of a marker and the potential for its use. The decision criteria here need not be too rigorous. High-risk groups, especially those identified in epidemiological studies, once notified of their risks, will have need for screening and counseling. The scientific and ethical concerns merge at this point and can be addressed by the same tactic. This tactic would provide for the test of a candidate marker in the high-risk group only as an adjunct to a more established monitoring or screening technique. Principles for selecting such techniques have been adduced.[17] The use of an established technique allows for some of the surveillance needs of the cohort to be met and for the cohort members to be told something about the results of the established screening technique with an acceptable degree of certainty. As for the experimental marker, the findings can be compared with the established technique to estimate the meaning of the findings. Using this adjunct approach, the need for rigorous criteria for prior evaluation of new markers is reduced somewhat. As a suggestion for an initiating criterion, markers should be tested in animals or humans until a believable hypothesis is generated. Then, as long as the test is not harmful to the subject, it could be administered along with the more established technique with little worry, in theory, as to any harmful effects.

Prudence and wisdom must be used in the implementation of this strategy and the explanation of the results. Still, high-risk groups, notified of their risks, are often likely to be willing to participate in such promising and altruistic research, and to accept the results of experimental tests, if presented honestly and in conjunction with more established approaches.

Cross-sectional testing of the various types of biomarkers will be of limited value, however. Markers for exposure and markers for effect that can be compared with established tests can yield immediate answers and indications of validity. On the other hand, markers of early disease, with nothing for comparison, will need to be tested in a prospective manner. The cohort will have to be followed and the predictability of the markers measured against disease end points. This is not as difficult as it might seem, because high-risk groups, once they are notified, need some kind of ongoing surveillance anyway. The prospective analysis of an experimental marker would not be that great an addition to the surveillance program.

This overview of a biomonitoring research strategy is preliminary and requires the combined input of laboratory scientists, clinicians, and epidemiologists, if it is to be fully developed and implemented in high-risk groups. The study of these markers should be accomplished by rigorous adherence to the rules of clinical research. The overriding objective of this research must be to move toward validating these markers as indicators of disease or exposure.

Societal Context

One cannot realistically speak of such screening and surveillance programs without identifying the social and political context in which they would occur. Notification and screening efforts do not exist in a vacuum, separate from the community. It is inaccurate to believe that these efforts will not be influenced by community pressures, particularly from the news media. In the Augusta study, more than 50 newspaper articles on the subject were written between 1980 and 1982. The articles dealt with the following major topics: (1) the prenotification delay, (2) notification, (3) the screening clinic, (4) funding for the future, (5) locating cohort members, (6) results of the study, and (7) litigation. Additionally, during that period a total of 58 reports were broadcast on the six- or 11-o'clock news, or the midday report. A half-hour, locally produced documentary entitled "Lethal Labor" was aired during prime time. In short, the notification of workers was officially initiated by letter, but the message was supplemented, amplified, distorted, or repeated by other groups. One lesson from all this is that in a notification effort, procedures must include plans for interacting with the news media and informing them of updated findings. In actuality, the news media perform the real notification.

At this time, social structures and programs are inadequate to support these interventions in high-risk groups, except in experimental or demonstration projects. Most state workers' compensation systems were not designed or reformed to accommodate the problems related to increased risk or resultant chronic disease with long latency.[18] Workers, once notified, are often in a "never-never" land between workers' compensation and their personal health insurance (if they have it).[1] Companies have been generally slow to embrace the needs of these groups and develop programs for entire "at risk" cohorts. This in part has been due to the nature of the cohorts and their geographical and historical dispersion. Workers often cannot get workers' compensation to cover screening when the disease is cancer resulting from exposures years earlier.[1,19] Once notified of risk, a worker's personal health insurance company is often reluctant to support surveillance and screening, arguing that this involves a work related disease. Even less available are services to deal with the social, economic, and mental health needs of such workers. It is no wonder that litigation appears to be the only appropriate route for these persons.

In Augusta, since 1981, 167 former employees have filed suits, seeking a total of $330 million. Of these 167, 119 cases have been settled (Augusta *Chronicle*, May 31, 1984, p 2B). Subsequently, the Georgia Supreme Court ruled that the plant owners could not be sued by employees who sustained bladder injuries from β-naphthylamine and that the workers must file claims under the state workers' compensation law instead (Augusta *Chronicle*, March 1, 1985, p 1A). It is not likely that the final settlement costs will be close to $330 million. Yet the litigation and attendant activities have affirmed the opinion that litigation and the workers' compensation approaches do not adequately respond to the multiple needs of workers notified of risk.[1,19]

In summary, screening and medical surveillance assume a pivotal role in a system that inadequately deals with the needs of workers identified and notified of

occupational disease risks. In some cases, ineffective screening programs are established because they represent surrogates for other kinds of support programs that do not exist in society today. To come to grips with this problem, the following guidelines are proposed:

1. The screening debate should be recast to include not only survival as a criterion, but an explanation of how screening serves to affect the quality of life of people at high risk of disease.

2. Screening and surveillance should be seen to include monitoring for disease markers and indicators of multistage transformations so that chemopreventive and behavioral modification efforts and other interventions can be promoted and evaluated.

3. A systematic and comprehensive program should be established to deal with the needs of workers at risk.

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Nurse-Midwife

In the last decade, some women and their families began to seek alternatives to hospital births. Some believed that the hospital setting contributed to the tendency to see birth as an illness rather than a natural process. Additionally, some decried the separation of a woman from her family at one of life's most joyous moments. In response, the natural childbirth movement arose and continues to grow. And midwives are playing an important role. In 1983, more than 100,000 babies, or nearly 3 percent of the year's total births, were delivered by midwives.

The Old English root of midwife means "with woman". This simple phrase applies to the modern practice of midwifery, for today's nurse-midwife is with her patient in the fullest sense of the word.

—From an interview by Michael Stanton of Marion McCartney in *Occupational Outlook Quarterly*, Spring 1986, p 36.