Ethical Considerations in Testing Workers for the -Glu69 Marker of Genetic Susceptibility to Chronic Beryllium Disease

Ken Silver, DSc, SM
Richard R. Sharp, PhD

Objective: *The most compelling real-world example of genetic testing for susceptibility to a workplace exposure involves those industries that process or fabricate beryllium. We examined ethical issues associated with testing for susceptibility to chronic beryllium disease.* ***Methods:*** *Using ethical and clinical criteria, we examined voluntary employer-sponsored testing programs in which individual results are reported directly to workers in a confidential manner.* ***Results:*** *Under reasonable assumptions, the longitudinal positive predictive value of the HLA-DPB1-Glu69 marker of susceptibility to beryllium disease is 12%. Interpretive challenges further limit the utility of the test and may inadvertently suggest a false sense of safety among workers. Concerns about confidential participation and pressures to be tested also must be addressed.* ***Conclusions:*** *Difficulties surrounding the interpretation of the HLA-DPB1-Glu69 marker, lack of assurance regarding the protection of worker confidentiality, and the potential lowering of social barriers to the implementation of mandatory worker screening combine to make testing beryllium workers inappropriate at this time.* (J Occup Environ Med. *2006;48:434–443*)

Unlike the administration of genetic tests in clinical settings, workplace testing often involves competing interests and agendas. Employers may be interested in offering or requiring tests to help minimize costs or reduce legal liability. By contrast, employees may pursue genetic testing because of health concerns, worries about the quality of their work environment, or in response to coercive pressures from employers. The conflicts of obligation that occupational health professionals routinely face in their efforts to strike an appropriate balance between the needs of both parties[1–4] may be especially profound in genetic testing.

How best to manage these competing interests has been a topic of much discussion for more than two decades.[5–9] To date, however, little consensus exists regarding the ethics of genetic testing in the workplace. We believe part of the explanation as to why progress has been slow in this area is that discussions have tended to focus on hypothetical examples of workplace genetic testing because few actual testing programs have been adopted by employers. In addition, the few genetic testing programs that have been conducted in the workplace have been extremely controversial, in part because the tests were based on questionable science.

In this regard, recent controversy over a genetic testing program administered by the Burlington Northern Santa Fe Railroad Company is illustrative of debates about genetic

From the Department of Environmental Health, East Tennessee State University, Johnson City, Tennessee (Dr. Silver); and Center for Medical Ethics and Health Policy, Baylor College of Medicine, Houston, Texas (Dr. Sharp).

Address correspondence to: Richard R. Sharp, PhD, Assistant Professor of Medicine, Center for Medical Ethics and Health Policy, Baylor College of Medicine, One Baylor Plaza, Room 310D, Houston, TX 77030; E-mail: rsharp@bcm.tmc.edu.

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testing in the workplace.[10–13] Faced with increased claims of work-related carpal tunnel syndrome, the railroad company hired a diagnostic laboratory to test claimants for sequence variations in the PMP22 gene, a gene associated with hereditary neuropathy with liability to pressure palsies (HNPP). HNPP runs in families and is extremely rare in the general population.[14] As a result, it was improbable that variations in the PMP22 gene would account for increased claims of carpal tunnel syndrome at Burlington Northern. Moreover, workers were not told they were being tested for this gene, nor were they told of the results. This suggests that the company's motives in developing this scientifically questionable testing program were related to legal efforts to contest causation in worker compensation claims and not to protect the interests of employees.

Testing programs like the one adopted by Burlington Northern highlight the importance of developing laws and policies to reduce the likelihood of employers conducting genetic tests of dubious value. Historically, occupational physicians and others engaged in medical surveillance in the workplace have enjoyed wide discretion in their selection of appropriate protocols and test methods.[15] This discretion has led to tests of uncertain value, both genetic and nongenetic, attaining routine use in the past.[16–18] In addition, the effectiveness of existing statutes and regulations designed to protect the rights of workers asked to participate in employer-sponsored genetic testing programs is unclear.[19]

If debates about the ethics of genetic testing in the workplace are to move forward, however, it also is important to consider the ethics of testing programs based on good science. Only by examining concrete examples of well-characterized biomarkers of susceptibility to workplace exposures can we define appropriate standards for determining when a genetic test is (or is not) appropriate for use in employment contexts. Policy debates that focus exclusively on problematic cases like the aforementioned Burlington Northern example present an incomplete account of the ethics of genetic testing in the workplace. A full description of the ethical terrain also should include an examination of circumstances in which testing workers for increased susceptibility to occupationally-induced disease may be more acceptable.

We believe the most compelling real-world example of genetic testing for susceptibility to a workplace exposure involves those industries that process or fabricate beryllium. In this study, we examined the ethics of testing workers for genetic susceptibility to beryllium sensitization and beryllium-related disease. Our analysis focuses on the specific circumstances in which testing programs are being piloted at this time, namely, as voluntary programs administered by third parties in a confidential manner. In focusing on this specific context in which genetic testing programs are being developed, our hope is to clarify salient ethical considerations in this "best-available-case scenario" in which there is substantial evidence to support the potential benefits of genetic testing in the workplace. Ultimately, however, we argue that these ethical considerations combine to make testing workers inappropriate at this time.

Occupational Disease and Workplace Exposure to Beryllium

As the second lightest metal known, beryllium and its alloys are used in a wide array of industrial applications, including the manufacture of aircraft components, dental materials, and golf clubs. In addition to these applications, the U.S. federal government has long been a major purchaser of beryllium for use in nuclear weapons, both as a neutron initiator and moderator. At least 66 private and public sites in 23 states handled beryllium for the U.S. Department of Energy (DOE) or its predecessor agencies since 1940.[20] At those sites at least 26,370 workers were exposed to beryllium,[21] and perhaps several thousand additional construction workers.[22,23] As of September 2003, among 21,137 current and former workers screened by DOE-funded medical surveillance programs, 685 (3.2%) had acquired beryllium sensitivity (BeS), a cell-mediated, antigen-driven immune response to beryllium.[24,25] Of these, 198 (<1%) workers have been diagnosed with chronic beryllium disease (CBD), which is a granulomatous lung disease. Case reports of BeS and CBD also have been reported in non-military contexts[26,27] and, in rare circumstances, civilian workers have developed the acute form of beryllium disease,[28] a chemical pneumonitis once believed to have been eliminated by industrial hygiene controls instituted in the 1940s and 1950s.[29]

A proportion of newly incident cases of BeS and CBD are believed to have resulted from airborne exposures that are less than the maximum permissible concentration of 2.0 $\mu g/m^3$,[29–32] raising concerns about the effectiveness of this standard. A study of BeS in beryllium–copper alloy workers exposed during the 1990s suggests that an adequately protective level may be closer to 0.01 $\mu g/m^3$,[33] or perhaps an 8-hour time-weighted average of 0.1 $\mu g/m^3$.[34] In its most recent occupational health standard for beryllium, the DOE has adopted an action level of 0.2 $\mu g/m^3$.[35]

Nothing but beryllium is known to cause CBD. Originally dubbed "berylliosis" because of its radiographic similarity to the pneumoconioses, CBD is now known to be mediated by responses of the innate and acquired immune systems.[36] The hallmark lesion of CBD is the noncaseating granuloma, detectable by lung biopsy, although granulomas may also occur at extrapulmonary sites.

A peripheral blood lymphocyte proliferation test (BeLPT) can be used to detect individuals who have developed BeS as a result of exposure to beryllium. Prevalence rates of positivity among beryllium-exposed workers generally are less than 10%.[37] The role of environmental factors, such as bioavailability, duration and intensity of exposure, and specific job tasks, is difficult to ascertain because of the lack of longitudinal studies with long periods of follow-up.[38] Medical surveillance practices call for the periodic reexamination of beryllium-sensitized individuals for signs of progression toward disease. Medical monitoring often includes bronchoscopy for biopsy samples to assess granulomatous changes in lung tissue. Lavaged lymphocytes frequently are collected during this procedure. A positive BeLPT in the lung compartment, along with granulomatous tissue changes, is viewed as providing a definitive diagnosis of CBD.[39]

CBD typically develops 6 to 10 years after exposure, but latencies as short as 4 months and as long as 30 years have been reported.[39] The clinical course of CBD is highly variable. Although a few cases advance to respiratory failure in a few years, the more common course of the disease is a long, gradual decline. Early symptoms include nonspecific respiratory problems, anorexia, weight loss, fever, night sweats, and joint pain. As the disease progresses, fibrosis of the lungs often is detectable by the use of x-ray.[40–42] Patient management typically involves treatment with corticosteroids and other available therapies for persons with granulomatous lung disease.[36]

The HLA-DPB1-Glu69 Marker of Susceptibility to Beryllium Disease

Several ongoing studies are exploring the extent to which interindividual genetic variability may play a role in the development of BeS and progression to CBD.[43,44] Among potential markers of genetic susceptibility to beryllium, the most significant predictive marker for the development of CBD identified at this time involves an amino acid substitution in one of the genes of the major histocompatibility complex. Richeldi and coworkers first showed that a glutamic acid substitution for lysine or arginine at position 69 in the HLA-DPB1-0201 allele is associated with an increased risk of CBD.[45] Subsequent occupational case–control studies have reported odds ratios ranging from 3 to 76 for the association between CBD and HLA-DPB1-Glu69.[46–48] Further work has established that HLA-DPB1-Glu69 is a supratypic marker with increased susceptibility associated with glutamic acid at position 69 in any of several HLA-DPB1 alleles, eg, *0201 *or* *1701, 0601, 0901, 1001, etc.[49,50] Attempts to elucidate the roles of specific alleles with respect to sensitization and disease progression have yielded mixed results.[47,49,51] The composition and structure of the beryllium–antigen complex have yet to be determined; however, several mechanisms and models have been proposed.[41,52,53]

Several studies have attempted to shed light on the interaction between the HLA-DPB1-Glu69 marker and environmental factors in the development of CBD. Richeldi and coworkers[48] evaluated the interaction of the marker and industrial exposure in a group of 127 beryllium ceramics plant workers. Forty-seven (37.0%) of the workers had job histories that involved machining beryllium, a factor known to be associated with increased risk of CBD.[31] Using logistic regression, the authors calculated odds ratios of 11.8 (95% confidence interval [CI] = 1.3–108.8) for the HLA-DPB1-Glu69 marker and 10.1 (95% CI = 1.1–93.7) for a work history involving the machining of beryllium.

The HLA-DPB1-Glu69 marker appears to have moderate-to-high sensitivity and low-to-moderate specificity. In five case–control studies, the marker has been present in 72% to 92% of subjects with CBD. However, only one of these studies was population-based[48]; therefore, these estimates of the marker's sensitivity must be interpreted cautiously. Studies of the specificity of the HLA-DPB1-Glu69 marker report that 30% to 45% of persons unaffected by BeS or CBD are positive for the HLA-DPB1-Glu69 marker.[45–47] In addition, the frequency of the HLA-DPB1-Glu69 marker varies across ethnic groups common to the United States.[54]

Workplace Testing Programs

At least two employers have provided voluntary testing for genetic susceptibility to beryllium-related disease to workers. The first is Brush Wellman, a leading manufacturer of beryllium. The second is Los Alamos National Laboratory in New Mexico (LANL), one of the largest users of beryllium metal and alloys in the United States. Although public information is scarce,[55] the scope of each programs differs. Brush Wellman piloted a program for new employees in which the genetic test was paid for by the company and administered in a confidential manner through an independent laboratory. Individual test results were provided directly to the worker, with no individually identifiable results reported to management. Genetic counselors were available before and after the testing by telephone.[56] Later, eligibility was extended to current employees of Brush-Wellman; however, company funding for the program eventually lapsed (D. Deubner, discussion at conference, Practical Approaches to Chronic Beryllium Disease, Denver, CO, January 17, 2003).

At LANL, genetic testing was provided through a research study of beryllium-exposed workers.[46,50] Initially, positive findings from this study prompted the development of a program to notify research subjects of results.[56] Plans also were made to offer the test to current employees who had been, or in the future are likely to be, exposed to beryllium (J. Williams,

memorandum to L. Anderman, LANL, February 7, 2002). Like the Brush-Wellman program, the proposed testing program at LANL would be voluntary and conducted by an independent laboratory, with confidential results provided directly to the worker. Genetic counselors also would be available to assist in interpreting results. A video that touches upon the genetic testing program was developed,[57] but it is unclear from publicly available information whether workers currently have the option to pursue genetic testing (either through a research protocol or through some other mechanism).[58]

At first glance, a program that offers potentially exposed workers the option to receive genetic testing on a voluntary, confidential basis would appear to be a "win–win" arrangement for all parties involved. From the worker's perspective, such a program would seem to serve employee interests in defining workplace risks while simultaneously limiting coercive pressures to participate and protecting against discriminatory treatment. From the employer's perspective, such a testing program may help reduce the incidence of disease, minimize costs related to poor health, and limit legal liability. Moreover, from the perspectives of occupational physicians and industrial hygienists, such a testing program would seem advantageous because it would provide a structured context in which to discuss worker concerns about occupational hazards and review job-related behaviors that may reduce exposure.

Several additional considerations combine to strengthen the case in support of such a workplace testing program. First, in contrast to the Burlington Northern case above, much is known about the HLA-DPB1-Glu69 marker of susceptibility to beryllium-related disease. Numerous studies have demonstrated that this marker is associated with increased risk of occupational disease, thus allowing genetic counselors and others to provide more informed estimates of the potential benefits and risks to persons considering the test. Second, CBD is an irreversible condition with significant long-term costs, both financial and human. If a genetic testing program could reduce the number of persons affected by the disease, it would be a much-welcomed development. Third, there is striking variability in human response to beryllium exposure, both above and below current regulatory standards. If genetic tests could reveal which individuals are at the most risk, they might permit more effective preventive interventions and more careful monitoring of persons at increased risk. Fourth, as noted previously, CBD is caused only by exposure to beryllium, a fact that simplifies the communication of results to persons who pursue genetic testing. Finally, unlike many other genetic tests, which frequently provide additional information beyond what the test is intended to reveal, very little collateral information is produced by tests for genetic susceptibility to beryllium disease.[59]

Ethical and Social Considerations

The strength of the aforementioned reasons in support of testing workers for genetic susceptibility to beryllium disease combine to make this an interesting case study for persons concerned with the ethics of genetic testing in the workplace. In what follows, we argue that the moral landscape is far more complex than it might initially appear, however, and that testing workers for genetic susceptibility to beryllium disease raises a number of troubling ethical and social issues.

Value Assumptions Implicit in Assessing Genetic Tests

Understanding a biological marker's quantitative properties is essential to the responsible implementation of a workplace testing program. In the early stages of marker validations, clear quantitative statements of predictive value may not be possible because of the highly provisional and uncertain state of knowledge.[60] If a marker is to be used in the workplace, however, some degree of quantitative clarity is required. Lacking this clarity, workers cannot be said to have made an informed choice about their participation in a testing program.

The question, however, is which of several numerical criteria is most salient in assessing the reliability and accuracy of a proposed genetic test. Placing emphasis on any one of the traditional criteria discussed herein—sensitivity, specificity, or positive predictive value (PPV)—reflects various normative assumptions about the objectives of genetic testing, acceptable rates of error, and the distribution of benefits and burdens associated with testing. Failure to be explicit about these assumptions denies elements of normativity surrounding the application of genetic information to disease prevention. Thus, it is essential to analyze the value assumptions implicit in these standard numerical criteria.

The PPV of a test is defined as the percent of positive test results that are true positives. It is a standard metric in clinical decision making. For a worker who has obtained a positive test result, the PPV provides an estimate of his or her likelihood of developing the disease. If the objective of a genetic testing program is to empower individuals to make well-informed decisions based on individual estimates of disease risk, then tests with high PPVs are desirable. In contrast, if the goal of a testing program is to reduce the proportion of individuals affected by the disease, as might be the case in a mandatory screening program, other criteria may be more pertinent to the assessment of a genetic test. For example, the sensitivity of a test and its ability to identify correctly persons at risk may be more desirable considerations in the assessment of a screening initiative.

If, as suggested previously, the HLA-DPB1-Glu69 marker of sus-

ceptibility to beryllium disease is moderately-to-highly sensitive, a large proportion of persons at risk for the disease would be identified as susceptible if the test were administered widely. If those at-risk individuals were subsequently removed from the workplace, either by their own actions or those of management, this would achieve a reduction in the proportion of cases of CBD. However, it does not appear that the testing programs piloted in the beryllium industry embody this logic since the removal of at-risk individuals is left to the discretion of those persons who volunteer to be tested and then subsequently choose to remove themselves from the workplace. Instead, existing programs seem to reflect a commitment to maximizing worker choice through the provision of individual information about disease risk. This suggests that the longitudinal PPV of the HLA-DPB1-Glu69 marker of susceptibility to beryllium disease is the critical metric to use in assessing the value of these testing programs.

The PPV of a test can be defined cross-sectionally or longitudinally, depending upon the design of the epidemiological study from which it is calculated.[61] To date, all estimates of the HLA-DPB1-Glu69 marker's PPV are based upon cross-sectional studies of beryllium workers. Cross-sectional estimates describe a test's ability to predict a worker's current disease status. To predict a worker's likelihood of developing disease *in the future*, however, well-designed multi-site cohort studies may be necessary. Such studies can provide disease incidence data on which to base reliable estimates of a marker's longitudinal PPV.

Proposals to offer genetic susceptibility testing for beryllium-related disease may rest on an unspoken assumption that the cross-sectional PPV of the test approximates its longitudinal PPV. In epidemiological terms, the assumption is that odds ratios calculated in cross-sectional studies can serve as adequate proxies for relative risks. This assumption is not unreasonable if the epidemiologic studies involved are truly population-based. To date, however, there has been just one population-based study of the HLA-DPB1-Glu69 marker.[48] In addition, the validity of the assumption depends upon whether a worker's current beryllium exposure status is an accurate surrogate for his or her past exposure. One's willingness to make these assumptions in the absence of empirical data may be a "hidden argument"[62] about the desirability of moving ahead with genetic testing in the workplace.

There are neither value-neutral, nor definitive standards for determining whether the longitudinal PPV of a test is sufficiently high to justify testing. However, such assessments need not be arbitrary. In part, what counts as an "acceptable" longitudinal PPV for the purpose of conducting genetic testing depends on the nature of the associated interventions and their potential risks and benefits. A high longitudinal PPV, for example, is imperative in clinical settings in which the resulting treatment is associated with significant risk.[63] By analogy, this suggests that if the HLA-DPB1-Glu69 marker is to be used in the workplace, its longitudinal PPV must be more clearly defined. In addition, because the potential social effects of the interventions associated with a positive test result can be quite significant, a moderate-to-high longitudinal PPV is required to justify workplace testing. Neither of these two conditions has been met to date.

Interpretive Challenges

Weston and coworkers[54] have estimated the PPV of the HLA-DPB1-Glu69 marker across a range of assumed values of relative risk, disease prevalence, and marker frequencies, assuming the marker's cross-sectional PPV can be used to approximate its longitudinal PPV. Using additional assumptions that bias upward the marker's estimated PPV (eg, a relative risk of 35, a disease frequency of 15%, and a marker frequency of 30%), they calculated a maximum PPV of 43%. Unfortunately, however, these assumptions do not reflect realistic conditions in the American workplace. The assumption of a disease prevalence of 15%, for example, is based on a study of machinists exposed to beryllium during the 1980s.[31] Beryllium-machining practices today, however, involve much more stringent controls to reduce exposures. For example, the beryllium facility at LANL seeks to achieve an operational goal of "zero" exposure through the use of numerous enclosed systems[64–66] and other techniques.[67–70]

We believe more realistic assumptions regarding the workplaces in which testing for the HLA-DPB1-Glu69 marker actually will take place suggest a disease prevalence closer to 5% and a carrier frequency of approximately 40% (where the latter value better represents the ethnic composition of one of the LANL facilities where the test has been offered). Under these assumptions, the PPV of the marker is substantially less (12%).

How this information is interpreted by those persons tested, and what significance it may carry for them, will depend on many factors. The difference between a 5% risk of beryllium-related disease (the baseline risk in this population) and a 12% risk of disease for those persons with the genetic marker may not be cause for action among many workers. This small numerical difference may be even less meaningful to more experienced employees already working in high-risk environments, particularly those who may have seen coworkers succumb to CBD in the past. Experienced workers may feel that the information provided by the genetic test tells them little that they did not already know.

A different interpretive concern is that a negative test result might prompt some workers to infer a protective effect and mistakenly assume it is unlikely they will develop beryl-

lium-related disease, when in fact the marker is absent from up to 25% of workers with CBD.[71] It is uncertain whether such a false sense of confidence would undermine ongoing workplace health and safety programs, but the possibility exists that a negative test result may cause some employees to be less careful in reducing occupational exposures, thereby endangering both their health and that of others in the workplace.

In addition, because test results are not available to management, individual workers bear the burden of interpreting the significance of these test results and making difficult choices about how best to respond to these findings. Perceptions of alternative work opportunities are likely to be important in these decisions. Where alternative work opportunities are scarce, a higher PPV may be needed to justify accepting the potential risk of long-term unemployment that a worker might face should he or she voluntarily leave or decline a job on the basis of test results. Where alternative employment opportunities are more abundant, however, beryllium-exposed workers may be more interested in a genetic test despite its low PPV.

One might also argue that voluntary workplace testing programs shift some moral responsibilities from the employer to the worker. For example, the availability of confidential tests for the HLA-DPB1-Glu69 marker may suggest to some that it is the worker's responsibility to get tested and, if necessary, remove himself or herself from the workplace if susceptible (as opposed to the employer's duty to establish a healthy work environment). To the extent that this perspective gains more acceptance, the resulting shift in the locus of moral responsibility will likely restrict, rather than increase, choices available to workers. Taken to an extreme, such a shift in public attitudes could lessen social and legal prohibitions against other forms of genetic testing in the workplace, for example, mandatory pre-employment testing or screening of workers.

Protecting Confidential Information

How best to protect the confidentiality of test results is a critical issue in the administration of all genetic tests.[72] In the context of beryllium-related testing, the rationale for these protections is that an employer or supervisor with knowledge of an employee's susceptibility might attempt to remove or transfer the worker from beryllium work areas, deny promotions to those work areas, or terminate the employee. To the extent that the legality of such actions is unclear,[73,74] the protection of confidential information about worker susceptibility warrants close attention.[75]

Direct disclosure of test results to management is unlikely given promises of confidentiality described in recruitment and consent materials. Nonetheless, deductive disclosure of worker identities may be possible. In the Brush Wellman program, for example, the test laboratory provides periodic summaries to the company. To the extent these summaries not only indicate the number of tests performed and the proportion of positive test results but also aggregate test data by department, period of employment, employee pay grade, and so forth, it may be possible to infer the identities of the workers tested. Moreover, deductive disclosure of worker identity is more likely in circumstances in which the numbers of eligible participants is small. If eligibility for susceptibility testing is restricted to small groups of workers with the greatest potential for exposure, for example, this possibility becomes more significant. Similarly, during periods of limited hiring or low workforce turnover, the identities of new participants may be more easily inferred.

Other threats to the confidentiality of test results may stem from the manner in which susceptibility tests are promoted. If there is much enthusiasm about the test in a particular worksite, employees may choose to reveal to others that they have been tested. Workers who discover that they lack the HLA-DPB1-Glu69 marker might believe their economic interests are best served by voluntarily disclosing this fact to their supervisor. If an attentive manager were to compare the identities of these self-disclosing participants against aggregate data provided by test laboratories, he or she may be able to deduce the identities of other workers who have been tested but have chosen not to disclose this fact to others.

It is doubtful that egregious breaches of confidentiality will be common in employer-sponsored genetic testing programs. Nonetheless, it is important that the format used in reporting aggregate test results be examined with regard to the potential for deductive disclosure. It also may be prudent to blind managers to some forms of disaggregated data, including the number of employees in a given work area who underwent testing and the proportion of employees found to have the HLA-DPB1-Glu69 marker. Minimally, participants should be counseled regarding the potential implications of voluntarily disclosing individual test results to management, friends, and others.

Ensuring Voluntary Participation

Despite good-faith efforts to ensure participation is voluntary, some workers will likely experience pressure to be tested for the HLA-DPB1-Glu69 marker. Some of these pressures will result from the mere availability of the test, which will force workers and their families to consider whether they would like the additional information provided by the test. Other pressures may result from the shifting of moral responsibility to workers discussed above. Still other pressures may exploit the inherent vulnerability of worker populations.[76] These pressures may be produced by the specific manner in which

the test is presented to workers at particular sites, the prior experiences of workers who have undergone testing at those sites, and the overall sense of the motivations of management in offering the test. To the extent that workers believe their employers are tacitly saying to them that they should be tested, the choice to undergo testing for the HLA-DPB1-Glu69 marker may not be fully voluntary.

Because voluntary participation is contingent upon management exercising restraint in its use of coercive power, it is appropriate to consider past experiences and institutional tendencies among those organizations proposing to test for the HLA–DPB1-Glu69 marker. In this regard, it is noteworthy that there is a long and troubling history of abuses of worker rights at Department of Energy (DOE) facilities like LANL.[77–80] This history of neglect and abuse[81,82] is still quite salient in the memories of many workers at DOE facilities.[83–87] For example, the human radiation experiments conducted by the agency's predecessor, the Atomic Energy Commission, have come to symbolize for many a widespread lack of respect for workers at DOE worksites.[88,89] These concerns continue today and are reinforced by allegations of retaliation against workers who raise health and safety concerns.[90,91] The introduction of genetic testing programs for beryllium workers takes place against this historic backdrop, thus highlighting the importance of transparency and openness regarding the motivations of persons of power in the beryllium industry.

Such considerations typically are not part of the assessment of a new genetic testing program.[92] Instead of examining the moral character of the agents or organizations involved in administering the test, assessments of a test's desirability usually focus on quantitative features such as the test's sensitivity and specificity. To a large extent, this reflects the fact that most genetic tests are administered in clinical contexts, where trust is often extended to persons of power. In the workplace, however, where shared interests and motivations cannot be assumed, the history of worker-management relations is an integral part of assessing the ethics of genetic testing. In the beryllium industry and in DOE facilities in particular, that history should prompt careful scrutiny of any new testing program.

These considerations suggest the need for open public dialogue regarding workplace testing programs involving the HLA-DPB1-Glu69 marker. This history also argues in support of requiring employers to provide high levels of assurance that testing programs will be conducted in a noncoercive manner with attention paid to ensuring voluntary worker participation.

We find little evidence of either these assurances or substantive labor and/or community involvement in the development of genetic testing programs in the beryllium industry. It is noteworthy, however, that the introduction of the nongenetic BeLPT test at DOE facilities during the 1990s provided experience in the development of research partnerships with worker organizations, scientists, and physicians.[93] One of these programs identified a need for workers to shape the procedures used to obtain informed consent for the BeLPT and policies for protecting worker privacy. Experiences in consulting affected stakeholders suggest that a participatory approach may be useful in assessing the desirability of genetic susceptibility programs as well.

Conclusions

Testing beryllium workers for the HLA-DPB1-Glu69 marker of susceptibility to CBD is the most compelling real-world example of the use of a genetic test to determine susceptibility to a workplace hazard. We have examined current and proposed applications of this test in contexts in which the test is voluntary and results are provided to workers in a confidential manner because those features further strengthen the case for testing. Despite the strength of the initial case in support of testing, our analysis suggests that it is inappropriate to test beryllium workers at this time.

The longitudinal PPV of the HLA-DPB1-Glu69 marker is too low to warrant offering the test routinely and the number of cases of disease that would be prevented by voluntary, confidential testing programs is unclear. In addition, there are interpretive challenges that further limit the utility of the test and may inadvertently result in less attention being given to industrial hygiene efforts. We also are concerned about the lack of clear guidance regarding the protection of worker confidentiality and procedures to limit the possibility of deductive disclosure of individual test results. These concerns, and additional worries about coercive pressures to undergo testing, are exacerbated by the fact that genetic susceptibility testing is being piloted in an industry with a long and troubling history of employee neglect and violation of worker rights. On the basis of these considerations, we conclude that the most effective, ethically acceptable way to achieve the goal of reducing the incidence of beryllium-related disease is not through genetic testing but through reduction of human exposure.

If we are correct in this analysis, our conclusion will be of much importance for ongoing ethical debates about workplace genetic testing programs. Because much is known about both the HLA-DPB1-Glu69 marker and the etiology of CBD, workplace testing for increased susceptibility to beryllium-related disease can provide a useful context in which to consider the ethical principles that should govern decisions about when to offer genetic testing in the workplace. If genetic testing is ethically troublesome in this "best-available-case" scenario, however, then testing workers for genetic susceptibilities to other workplace hazards will likely be problematic as well.

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