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Occupational Risk Assessment and Genetic Testing in the Workplace

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Abstract

In order to reduce workers compensation cost and to protect at risk employees, employers are considering using genetic testing in the workplace. If genetic testing is used, employers need identify specifically the disease that is associated with the exposure and may need to consider personal habits of the employee that contribute more to an employee's health status. There are legal ramifications in both the United States and internationally to genetic testing that both the employer and the employee may consider.

Keywords: Genetic testing; Risk assessment; Genotype; Disease/illness; Chronic beryllium disease; Alpha-1 antitrypsin; Medical surveillance

Introduction

There are approximately 166 million workers in the United States at a present time [1]. Of these 166 million workers, there were approximately 207,500 workers diagnosed with an occupational related disease/illness in 2011 [1].

An occupational related disease or illness is any disease or illness that is directly attributable to an exposure in the work environment. A disease or illness may be considered work-related if there is a preexisting condition that is aggravated by an exposure in the work environment. An issue, however, the number cited, 207,500, does not reflect if the disease or illness is from an acute exposure or from a chronic exposure. If any worker, despite the worker's genotype, experiences an acute exposure to chlorine gas via the pulmonary route, there will be damage to the lungs. If a worker is chronically exposed to coal dust, even if he wears a respirator as prescribed, but smokes cigarettes, this will hasten pulmonary disease.

Risk assessment is a scientific method used to determine an individual' risk of developing a specific adverse health effect due to a specific exposure [2]. There are four components to risk assessment or management. The first is hazard identification, which is based on *in vitro* tests, animal bioassays, and epidemiological studies. The second component is the dose-response assessment that includes susceptibility, age, and the gene-environment. The third component is the exposure assessment that investigates the types, levels, and the duration of exposures. The final component is the risk characterization that examines the nature of the risk, estimates the adverse effect of the worker, examines the robustness of the studies from the hazard identification, the susceptibility of the population, and the relevant of the mode of action [3]. Occupational risk assessment measures the risk factors for a specific disease from a specific exposure among individual workers.

Genetic testing may be considered as a tool to reduce the number of occupational related illnesses and diseases. Genetic testing may be used to detect the presence of a specific genotype that may increase the risk of developing a certain disease in an otherwise healthy individual. Employers may consider using genetic testing to exclude those employees from areas that may increase their risk of developing an occupational related disease and thus reduce workers' compensation cost and keep at risk employees healthy.

Employers may use two types of genetic testing in the workplace: genetic screening and genetic monitoring. Genetic screening is used to determine a specific genotype that may increase an employee's risk of disease but the disease may not be associated with any workplace exposure. Genetic monitoring is used to evaluate an employee's change in genetic material that is specifically due to an exposure at work, for example, radiation exposure. This may provide an employer the knowledge that may be used to develop new safety standards that may ultimately to reduce or prevent the risk of disease [4].

Genetic testing is controversy and may not be a predictor of a given disease. According to the Department of Labor, genetic testing may be used to discriminate against highly skilled workers and access to better paying positions. There is a racial component to genetic testing as well, for example, African-Americans more likely to posses the sickle cell trait and yet live healthy lives, but may be stigmatized by possessing the sickle cell trait. The Human Genome Project has revealed that there may be 50,000 to 100,000 genotypes with an estimated 3,000 to 4,000 that may be responsible for disease [5,6]. It is uncertain, however, if any of these genotypes alone, are responsible for developing certain disease. Factors such as environment, personal habits, and lifestyle may play a larger role in the development of a certain disease.

Pre employment physicals are a routine part of employment screening. Pre employment physicals may require specific laboratory test, such as cholinesterase testing for those workers who will be exposed to organophosphates. There is a caveat as per cholinesterase testing. Workers that have a genetic history of pseudocholinesterase deficiency will show abnormal levels of cholinesterase upon pre employment screenings and then a fitness for duty may be considered. Employees are also subject to medical surveillance that require periodic laboratory testing, e.g., blood lead levels. If periodic testing reveals abnormal values, the worker will be relieved of his regular duties until further testing can be done and laboratory values return to acceptable levels.

Baseline and periodic laboratory testing is legally mandated by federal and state Occupational Safety and Health laws, however, genetic testing is not. Baseline and periodic laboratory testing are done to protect the worker from acute and chronic diseases associated with

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a given workplace chemical. Genetic testing is being marketed in the United States to employers with the same rationale.

However, genetic testing in the workplace may not provide an accurate assessment of the risk to a worker. Workers may have other risk factors such as smoking or obesity that may contribute more to development of an occupational disease or illness. Genetic testing for a specific genotype continues to have limitations as to the predictive value of developing the disease but may provide information as adequate exposure limits by examining individual susceptibility [7]. Risk assessment may be vital part of an employee's health evaluation. Occupational risk assessment is done to determine personal risk factors that may increase an employee's likelihood of developing an occupational related disease or illness. Genetic testing may not provide adequate information as to the risk of developing, for example, chronic beryllium disease, but in some cases, such as the risk of developing pulmonary disease, genetic testing for alpha-1 antitrypsin may be indicated.

Beryllium is a toxicant that is used nuclear industrials and aerospace industrials. Beryllium exposure, acute or chronic, may lead to serious health consequences. Chronic pulmonary exposure may lead to chronic beryllium disease that may lead to a systematic granulomatous disease. Acute pulmonary exposure may cause a pneumonitis. Medical surveillance is mandatory and requires workers to have a lymphocyte proliferation test. The lymphocyte proliferation test is a blood test that measures the beryllium antigen-specific cell mediated response [8]. If there is a lymphocytic response, then the worker has been sensitized to beryllium and may develop chronic beryllium disease. The lymphocyte proliferation test is a highly specific tool to assess chronic beryllium disease; however, due to the length of time needed to run this assay, exposure to radiation of the workers that are performing the test, and the potential for variability with interpretation, there is still a need to develop more efficient methods [9].

A genotype has been discovered that may identify those workers at risk for developing chronic beryllium disease. This genotype, HLA-DPB1-Glu69, may be a biomarker for genetic susceptibility. Ninety-seven percent of the workers diagnosed with chronic beryllium disease have the biomarker Glu69, however, 30% to 45% of workers with the biomarker Glu69, that were exposed to beryllium did not develop the disease [10]. Wang et al. speculate that the workers who were diagnosed with chronic beryllium disease had a specific allele, 0201 Glu69 [10].

However, HLA-DPB1 Glu69 was later determined that it may be a biomarker for sensitization or the initial immune response, but may not be a biomarker for the development of chronic beryllium disease [11]. It is speculated that it is the cytokine production from the immune response that leads to chronic beryllium disease. The authors suggest that further studies need to be done to investigate the gene-environment connection in the development of chronic beryllium disease.

Increased exposure to beryllium triggers a type IV antigen-specific cell mediated immune response that is associated with a specific genotype. Personal risk factors such as asthma, smoking, or history of sarcoidosis did not contribute to development of chronic beryllium disease; however, information on these risk factors is limited. One study did suggest that smoking did not increase the risk of development of chronic beryllium disease [12]. However, there may be a link between smoking and beryllium exposure to the development of lung cancer, copd, nervous system, and urinary tract cancers [13]. A study by Boffetta et al., found there was no causal association between smoking and beryllium exposure and the development of lung cancer [14].

With the example of beryllium, there appears to be a specific genotype that is associated with sensitization of beryllium but it is unclear if there is a specific genotype that is associated with the development of chronic beryllium disease. However, genetic testing could not provide information as to exactly what threshold limit levels that would be adequate to prevent sensitization and the development of chronic beryllium disease. Genetic testing in this case could not provide any risk assessment with regard to the development, for example, of lung cancer and the association between beryllium exposure and smoking.

Alpha-1 antitrypsin deficiency is an inherited genetic trait that is associated with an increased risk for developing lung disease [15]. A single gene with two common variants, the S variant, codes alpha-1 antitrypsin deficiency known as Glu264Val and the Z variant, known as Glu342Lys. The Z variant is associated with an increase risk for disease, whereas, the S variant has not been associated with any disease disorder [15]. A deficiency of alpha-1 deficiency allows neutrophil elastase to breakdown lung tissue that leads to airway hyperresponsivenss that is exacerbated by environmental irritants such as cigerettes.

Workers, such as firemen, coal miners, or bakers that are placed in dusty work environments are at an increased risk for developing pulmonary disease. Outside risk factors that greatly influence the development of pulmonary disease in these workers are smoking or a personal history of asthma. There are numerous cases of rescue workers from the World Trade Center terrorist attacks that have an history of alpha-1antitrypsin deficiency and due to the exposures of dust during the attacks, have developed pulmonary disease [16].

Genetic testing for alpha-1 antitrypsin may be considered because of the increase risk for pulmonary disease, but employers would also need to consider the personal habits of the employee as well as the compliance with personal protective equipment. Employers may need to consider using threshold limit values that are recommendations provided by the American Conference of Government Industrial Hygienist that are based upon lifetime toxicity levels and are considered more protective versus the Occupational Safety and Health permissible exposure levels are time weighted averages over a specific period of time in which a worker may be exposed to a higher concentration during a short period of time.

There are no federal or state laws in the United States that mandate genetic testing; however, there are laws that are enacted to protect employees. The Equal Employment Opportunity Act is a federal law that protects workers against discrimination based on age, sex, or ethnic background. The sickle cell trait is uniquely associated with African-Americans, under the Equal Employment Opportunity Act; employers may not discriminate against African-Americans because of the possibility of possessing the sickle cell trait and even if the employee does have the sickle cell trait, the genotype may not contribute to the risk of developing an occupational disease. The American Disabilities Act prohibits discrimination against workers with physical or mental limitations, however, the law may be overturned if the employer cannot reasonable accommodate the worker that would otherwise place the worker at increased risk of injury. At the present time, employers are able to have unrestricted access to an employee's health record after an employment offer is made [4].

There are two other federal laws that employers have to consider. The Genetic Information Nondiscrimination Act of 2009 states that an employer is not able to inquire any genetic test until after the job offer [4]. The Health Insurance Portability and Accountability Act of 1996,

was established to protect the privacy of an individual with regards to personal health information [4].

At the present time, there has not been any court cases' involving genetic testing and employment. However, there was a notable court case the involved the American Disabilities Act. In the court case of Echazabal vs. Chevron, the plaintiff, Mr. Echazabal was denied employment because of his hepatic C status. Mr. Echazabal sued Chevron under the American Disabilities Act. The plaintiff applied for a position at Chevron that involved working with known hepatic carcinogens. Mr. Echazabal was denied employed because he was at increased risk of developing hepatic cancer due to his underlying liver disease. It was the opinion the Supreme Court, that the Chevron Corporation could not reasonable accommodates Mr. Echazabal from harm and therefore, ruled in favor of the Chevron Corporation [17]. The concern with the Echazabal case was that if there is a specific genotype that is associated with a specific occupational disease, the employer may deny employment based on that the employer may not be able to establish any safe threshold levels for an at risk employee.

There are no specific guidelines that an employer can use but it is recommended that employers should not require genetic testing in the workplace as a condition of employment, should not be used to discriminate in a way to deny employment opportunities, and should avoid obtaining genetic information. However, an employer may permit genetic testing to monitor the health of an employee when there is a workplace exposure that may cause genetic damage and use genetic testing to control adverse working conditions and to prevent harm to the employees. It is the obligation of the employer to maintain confidentiality of medical records and provide informed consent [4].

Internationally, the debate as per the effectively of genetic testing and the concerns for privacy continues. There are no specific laws that detect genetic testing in the workplace, however, the International Labor Organization raises concerns that genetic testing may be used as a form of discrimination and states that employers should not use genetic information to discriminate against workers deemed high risk since there is evidence that genetic testing has been used to discriminate against those patients planning to purchase life insurance [18]. In Australia, for example, genetic testing is being used to determine at risk cancer patients, but in the workplace, there is an ongoing debate that genetic testing may be used to protect employees and that genetic testing should only be used when there is a high probability that a specific occupational disease will develop in a specified period of time [19]. In Germany, there appears to be little interest in occupational genetic testing, however, genetic testing is used in the practice of medicine, for example, in the case of cystic fibrosis [20,21].

Genetic testing in the workplace may provide information that may identify at risk populations. Information may be provided as to specific threshold levels to protect at risk employees with genetic susceptibilities. However, genetic testing may not be a single risk assessment tool to identify at risk employees. Employers may consider, for example, personal risk of the employee. Smoking and obesity may contribute more to disease than the chemicals in the workplace. There is a fear that if an employee is deemed "at risk," he or she will be denied employment opportunities. This may also set precedence for employers to deny employment to other at risk populations such as smokers and the obese, even though in the case of beryllium, does not contribute to the development of chronic beryllium disease. Alpha-1 antitrypsin deficiency, on the other hand, has a strong association between developing pulmonary disease from environmental sources. There is also concerned that if employees are provided with genetic testing and are deemed "low risk," that these employees would not be compliance with safety protocols even though this topic has not been well studied. There continues to be a debate both in the United States and internationally as per the effectively and efficiency of genetic testing in the workplace, as well as concerns of discrimination and privacy.

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