GENETIC SCREENING — AN ABSOLUTE NECESSITY OR A MISCONCEPTION?

JANUSZ HANKE, MD, PhD and JANUSZ A. INDULSKI, MD, PhD

Nofer's Institute of Occupational Medicine, Lodz, Poland

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Abstract. The authors present arguments for and against genetic screening during preemployment examination and state that most genetic tests have not been verified by epidemiological studies. Social and ethical aspects make up the majority of arguments against genetic screening. The main argument in favour is that hygienic standardization does not protect all workers who exhibit susceptibility higher than normal and does not provide efficient health safety.

The range of human diseases and abnormalities varies from one extreme, that of inherited disorders, with all individuals who have the appropriate genes developing the condition, to the other, that of typical environmental diseases. Between these two extremes there occur various disorders in which both genetic and environmental factors are conspicuous. Only a small segment of the population which is both genetically predisposed and subject to unfavourable environmental conditions does actually develop a clinical disorder. A characteristic example of the way in which environmental and genetic factors may interact in the causation of a disease process can be found in pharmacology. Pharmacogenetics and ecogenetics are two scientific disciplines which explore the problem of genetic predisposition to drugs and environmental agents. Pharmacogenetics started to develop in the mid-1950s, when the differentiation of effects provoked by therapeutic doses of suxamethonium in a group of human beings was found to be genetically determined. Today, pharmacogenetics is no longer a field in which extraordinary reactions to drugs are being discussed, but instead, it has started to be a discipline of major significance for pharmacology and toxicology. The introduction

Address reprint requests to J. Hanke, Nofer's Institute of Occupational Medicine, 8 Teresy Street, 90—950 Lodz, P.O.Box 199, Poland

of genetic concepts to experimental pharmacokinetics seems to be very promising for arriving at interesting data in the future. Recently, some ideas from pharmacokinetics were transferred to environmental studies. In 1971, the term "ecogenetics" was used for the first time in Brewer, as cited by Motulsky (10). Ecogenetics is concerned not only with toxic agents but also with teratogenic, mutagenic and carcinogenic substances. However, the list of research works analysing genetically influenced variations in response to environmental agents is still very short. Ecogenetic problems will perhaps inspire the specialists working on questions of occupational health and industrial toxicology.

The year 1987 marks a quarter of a century since the first attempts were made to identify workers with a genetic potential of hyper-reactivity to industrial chemicals (16). It has been suggested that the tests for detecting workers who are hypersensitive to industrial chemicals should be applied during the job preplacement examination in order to assign a given job according to the innate individual characteristics of the workers and, thus, to reduce unnecessary health risk.

In 1987 we edited the first book, "Genetic problems in toxicology and occupational medicine" (authors: J. Hanke, J. Indulski, J. Pawlak) in which, under one cover, a large amount of information concerning pharmacogenetics and ecogenetics derived from the newest ample world publications was collected.

According to Stockinger and Scheel (18), who prepared a consensus report, the prerequisites for a hypersusceptibility test in industry must fulfil the following conditions:

1) The abnormality or deficit must exhibit a relatively high prevalence in the working population.

2) The test must concern substances commonly occurring in industry.

3) The condition must be compatible with an apparently normal life before industrial exposure occurs.

Following these prerequisites it has been suggested that some abnormalities should be introduced in industrial screening: alpha-antitripsin deficiency, glucose-6-phosphate dehydrogenase activity, reagenic antibodies to allergenic pollen antigens in "hayfever" occurring in certain industrial chemicals and found in the sickle-cell trait. Reception of the hypersusceptibility tests in industry was extremely unfavourable in the United States and Canada. The tests were also used in other industrialized countries. The reasons were economic, social and scientific. From the economic point of view, time and expense were the factors. Medical departments could not obtain funds to maintain the screening programme. Most European countries do not have a large black workforce. Hence,

two of the most frequently applied tests, the glucose-6-phosphate dehydrogenase and sickling tests are of little or no importance.

Social factors appeared exceptionally important. In 1981 in a four-part series in "The New York Times", the issue of genetic screening of individuals prior to entry into the workplace of certain industries was evaluated (15). According to the opinions presented, the policy is highly controversial, with numerous social, legal, medical and economic implications. As a result of "The New York Times" series a genetic bill designed "to eliminate genetic screening of employees in the New York State" called "The Genetic Testing and Employment Act" has been proposed. This bill would prevent employers from "requiring or suggesting employees or prospective employees undergo any form of genetic test for the purpose of considering employability, except when requested by the employee or authorized by collective bargaining agreement". In addition, the proposal bill would prevent employers from disciplining employees who choose not to be tested; it would provide civil penalties against employers who transgress the law, and prevent the issue of result of genetic testing without the employee's permission.

The arguments supporting the bill were:

1) the notion that "employees have weak or defective genes" is a repugnant invasion of the individual's privacy,

2) the hazard, not the workers, should be removed from the workplace,

3) there is a strong likelihood that a screening programme may be a subtle form of radical discrimination (4).

The bioethical problems connected with job preplacement examinations have been studied by Motulsky (10). According to this author, the practical application of the suggestion that the testing may aid job assignment by considering the innate, individual characteristics of a worker, thus reducing unnecessary health risk, should not be promoted. A situation may develop in which a harmless deficit of an enzyme or a protein could be used as an argument to discriminate racial or ethnic groups with high frequencies of such deficits. So, in the opinion of some authors (12), there is no foundation for suspecting that the individuals with sickle-cell trait are predisposed to adverse effects from chemical exposures to nitro- and aminoaromatic compounds (14) or to benzene, cadmium, lead, carbon monoxide and cyanide (16).

According to the opinion of some authors, the scientific background of genetic screening is not sufficiently satisfactory to justify the practical action. Let us analyse two fundamental arguments:

1) It is well known that susceptibility to toxic agents is highly affect-

ed not only by genetic determinants but also by age and nutrition status, as well as the presence of preexisting diseases and life-style (3, 5).

2) There are suggestions that a biochemical deficit or an abnormality which is looked for during genetic screening is not important in itself, but simply acts as a marker of families who can be predisposed to harmful environmental effects (9).

When considering the current state of the genetic screening problem it is worth to quote the reasonable assessment by Cooper (7): "There is insufficient epidemiologic evidence to support the use of any hypersusceptibility test as a criterion of employability without many qualifications. On the other hand, there is ample scientific evidence to support wider testing. Premature assumptions as to the necessity of such tests, or over-optimistic claims, impede testing. It is known that no employer should be regarded as liable or derelict for not choosing to screen his employee. If he screens all employees, he would have to consider whether he would be regarded as liable to criticism for using a positive test to deny employment, or conversely, for jeopardising the health of an individual permitted to work with a positive test".

Nevertheless, genetic screening is inevitable in the future. First of all, it is becoming more and more clear to those who examine the response to worker's exposure that there is a wide range of susceptibility among workers even under carefully monitored exposures. Recently Cartwright et al. (6), reported an extensive study on the predispositions of slow acetylators to occupationally induced bladder cancer among the workers employed in the dye-manufacturing trade in Huddersfield, a heavily industrialized town in the Yorkshire region of England. The prevalence of bladder cancer among the population in study is twice that in the United States and among the highest known in the world. Before 1952 the workers were exposed to 2-naphtylamine and up to 1960 they were exposed to benzidine. There is only a small excess of slow acetylators among the total group of Huddersfield patients with bladder cancer. However, among the dye-workers with bladder cancer 22/23 were slow acetylators, in contrast to patients with bladder cancer who were allergic, or engineers using machine oils (40% and 44% slow acetylators, respectively).

The recognition of highly susceptible workers would enhance preventive services and diagnostic management for these individuals and might even focus more specific attention on the environmental conditions in the host-environment interaction. For the physicians who find symptoms in workers it is essential to try to answer patients' questions concerning personal susceptibility. Too often the environmental problem may go unnoticed because it is so infrequent in the overall population

of workers, or because careful studies of affected workers are not conceived and performed (13).

Secondly, there is no provision in many, if not in most industrial air standards, which would provide protection for all workers; the hypersusceptibles commonly respond to exposures well below the limit set by the standards (17). Soon after OSHA was founded, it adopted all the threshold limit values (TLV) of the American Conference of Governmental Industrial Hygienists (ACGIH) for non-carcinogens as its standards (2). The preface to the TLV booklet of the ACGIH specifies these TLV-s as the ones which may not offer an absolute protection to those at enhanced risk (1). Consequently, it follows that by adopting the TLV-s of the ACGIH as 'de facto' standards, OSHA decided not to take into consideration those who may be at an increased risk. Thus, a company may be in absolute compliance with the standards, and yet not protect some workers classified as high risk (4). In this situation, in addition to environmental controls and work practices, an elaborate array of preplacement and periodic postemployment examinations should be requested. The Environmental Protection Agency (EPA) has specified an explicit treatment for the identification of the groups which are likely to be highly susceptible. Individuals with asthma and emphysema and young children were highly susceptible to the ozone standards and the airborne lead standard, respectively. The EPA declared that the proposed standards would indeed be protective for such subgroups, and for those with a margin of safety left (8, 11).

It is necessary to give an impetus to scientific research and epidemiological studies to clarify the genetic background of hypersusceptibility and to prepare screening. It is also important to find a person or an institution to initiate an explicit arrangement to permit research investigations and to specify the use of and access to data. Moreover, all participants should recognize the difference between penetrating, genuine research and potential subsequent application of the tests, validated for routine screening and surveillance.

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