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Acceptability of genetic susceptibility testing in occupational health – a position paper

by

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Abstract

Assessing the acceptability of genetic testing practices in occupational health can only be done in relation to particular goals of an occupational health policy. If protecting both health and employment of every job candidate and employee is the aim, the assessment of the relevance, the accuracy, the need for, and the consequences of these practices reveals that according to the current state of knowledge, there is no reason to believe that pre-employment selection practices based on genetic screening test results could be part of a rational policy, aiming at protecting workers health. The main reasons are the lack of predictive value at the individual level and the possibly paradoxical effects for health protection, both at the individual level of the candidate who will be refused a job and at the level of the employees who might wrongly be considered as risk-resistant. The decision making process requires societal involvement.

Keywords: *Occupational health, genetic susceptibility, ethics, informed consent, chronic beryllium disease.*

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Introduction

Although genetic tests are not yet relevant for predicting occupational diseases, there is a growing demand for genetic susceptibility testing in occupational health. The possible consequences for job applicant and employee of the introduction of genetic tests in occupational health are a reason for societal concern. Depending upon their use, they may contribute to well-being, but may also lead to social exclusion.

A *conditio sine qua non* for acceptability of any test used in occupational health practices is that it can contribute unequivocally to the protection of the employee. This applies also to genetic testing. An open discussion about the use of tests should cover several questions that reflect scientific, social and ethical issues and that relate to the relevance, the accuracy, the need for and the consequences of a testing practice[1]. These questions address a.o. the severity of the disease to be avoided and its relation with occupational risks; the degree to which a test result predicts disease outcome and the extent to which

[1] The **relevance** of a practice to its objective is the degree to which it gives useful information about the problem under consideration; e.g. the extent to which a particular susceptibility factor or early effect marker predicts a disease or the severity of an effect.

Accuracy depends on validity and reliability. Validity is the extent to which the practice assesses what it is intended to assess e.g. the extent to which a test for a particular trait or factor identifies all persons with that trait or factor, and only them. The most useful parameter for describing the performance (validity) of a test in a population is its predictive value (PV): the proportion of people considered to be positive who are true positives. The PV depends on the prevalence of the risk factor in the screened population. Reliability is the reproducibility of a result or the degree of similarity among results when the practice is repeated under similar circumstances. Reliability depends on the variability of the manifestation on which the test is based and on the variability of the method of measurement and the skill with which it is done.

'Need/necessity' refers to the extent to which the presumed objective of the practice can be met in a different way. This aspect might also be termed 'subsidiarity'. It includes an evaluation of whether the practice is necessary to obtain the information, or whether the information could be obtained e.g. by another test, by interview or by clinical examination. It also includes an assessment of whether (or to what extent) the information is needed in order to reach the objective, i.e. whether the information is an essential element that is irreplaceable by other means for the objective to be met. For instance, primary prevention combined with adequate medical surveillance could make a particular selection test superfluous in preventing an occupational disease.

The **consequences** of selection and surveillance practices can be direct or indirect and may be related to the individual job applicant or worker, their relatives, other workers and society. In order to study consequences, the medical use of the results of a test (criteria for exclusion from a job, definition of cut-off points for positive results) and the socio-legal consequences of the medical decision are to be analysed at the individual level, at the level of the work force as a whole (including unemployed people) and at the level of society (1).

people having the genetic or other risk factor are at higher risk for developing the disease than people who do not have it; the number of people that could be wrongly excluded or wrongly included; the relevance and achievability of other measures to reduce the risk; the social consequences of the test results and the protection of privacy. The questions are interrelated: the answer to one will determine the cut-off point for answering another one. The answers will differ, however, according to the social and ethical principles applied (1,2,3).

An example may illustrate the social impact testing for genetic traits in workers may have. Beryllium is known to cause chronic beryllium disease (CBD). Beryllium is a metal found as a component of coal, oil, certain rock minerals, volcanic dust, and soil. Elemental beryllium is the second lightest of all metals and is used in aerospace, nuclear, electronic and manufacturing industries. CBD is an immune system – mediated pulmonary disease involving chronic inflammation / fibrosis. Genetic analyses demonstrate regions of high variability in genes encoding for the receptors that play a primary role in recognizing beryllium and initiating the immune response. Epidemiologic studies have demonstrated some associations between specific genetic variants of these genes and the risk of developing disease. In one study beryllium exposed individuals with the HLA-DPβ1-Glu69 genotype had an eightfold increased risk for CBD, compared with individuals without the genotype. The prevalence of the HLA-DPβ1-Glu69 genotype was approximately 30 % (4).

Assuming an eightfold increased risk for individuals with the HLA-DPβ1-Glu69 genotype, an incidence of 50 CBD cases among 1000 relatively highly exposed workers, and assuming that the workers with the Glu69 genotype are identified with a perfect screening test and selected out, it can be calculated that the number of CBD would be reduced from 50 per 1000 workers in the unscreened workforce to 16 per 1000 workers in the screened workforce. In this hypothetical scenario using relatively high figures for absolute risk and for relative risk, it may look as if potential benefits of genetic screening are high. However, when assessing acceptability, one should take into account the costs and consequences of such practices: e.g. in order to find 1000 workers without the susceptible gene variant, a total of 1429 workers should be tested, 429 of whom would thus be refused for employment (5). Moreover, of these 429 workers refused, 87% would never have contracted the disease if they would have been accepted for the job. Also, in real-world scenarios, tests are not 100% accurate. Screening errors in general will increase the number of people tested, and decrease the difference

between the number of disease cases with and without screening. The need of selection may be questioned as the primary means of reducing disease incidence should be exposure reduction efforts.

Limited relevance of genetic testing

Hitherto there are no genetic tests available which are capable of distinguishing accurately between employees with greater susceptibility to certain serious occupational risks and those who are less susceptible. It is not possible yet to predict accurately future health problems which may result from the working conditions.

There are various reasons for this state of affairs.

- The genes already studied represent only part of the inherited factors and not more than a fraction of the other (acquired) susceptibility factors which, in an extremely complicated manner, all combine to determine the susceptibility to an occupational illness.
- There are many variants of the genes already known. In addition to the 'wild type' there is an amalgam of different mutations, some of which are not yet known and cannot therefore be tested. Nor is the significance of each of these variants for the susceptibility to occupational diseases known as yet.
- The tests for known genes are not always 100% accurate. In other words some tests do not correctly identify all carriers of a certain gene, and only them.
- The effect of genetic susceptibility factors can change considerably depending on the level of exposure. This effect may even be directly inversely proportional with the exposure (the greater the exposure, the smaller the difference in risk) (6, 7, 8). Our knowledge of this relationship between exposure and genetic susceptibility is however still very limited.

At present, therefore, results of genetic tests do *not* form a reliable basis for excluding potential employees from certain jobs to prevent occupation-related illnesses (9, 10, 11).

Distinction between genetic screening and genetic monitoring

In the societal debate about the acceptability of genetic tests, a clear distinction must be drawn between genetic tests which are intended to detect inherited characteristics, which may point to greater *susceptibility* to certain conditions (genetic screening) and genetic tests which aim

to find *changes* in the hereditary material, which *are the result of* exposure to harmful substances (genetic biomonitoring).

Genetic biomonitoring can form part of the periodic medical examination carried out on employees and is specially designed to assess the *effects* of exposure to (carcinogenic or mutagenic) agents in the workplace. The results of genetic monitoring can lead to the unearthing of unknown, but hazardous types of exposure. Better knowledge of genetic susceptibility to occupational diseases can contribute significantly to more effective medical surveillance of workers exposed to risks. Such knowledge will lead to better interpretation of the results of biomonitoring tests (1, 10).

Protective and preventive role of occupational medicine

Practices in occupational medicine should not be based on employee selection but on social protection. The goal of occupational health practices and surveillance must be to ensure that work is adapted to man and not the other way round. In other words, other methods of risk control such as improving working conditions together with health surveillance through periodic medical examinations will be preferred above excluding people from work. However, the tradition of simultaneous protection of the right to work and right to health protection threatens to come under pressure in the current socio-economic context in many industrialised countries. On the one hand risk-related work is being turned down by large companies and is being out-sourced to smaller companies with a high staff turnover, less controlled working conditions and only the fittest remaining. On the other hand policies for the protection of employee health and safety are increasingly reduced to a number of generalised norms or standards to comply with. This development can create serious problems for the organisation and efficiency of health surveillance and can reduce social protection, especially of the weaker. Furthermore, the existing regulations on recruitment examinations are insufficiently enforceable because of gaps in the current legislation in many countries.

In Belgium the legislation has recently been adapted, in order better to protect job candidates against unfair discrimination for health reasons, by setting a series of rules which allow occupational medicine to fulfil fully its mission of social protection. Employers have no access to medical data and are not entitled to ask for medical information. Solely the occupational health physician – who's status and role are strictly prescribed by law – performs medical examinations for workers. Tests are allowed

only in so far as they are related to the current fitness for the job. The use of genetic tests is forbidden in the field of occupational health, except if they are imposed by Royal Decree in very specific circumstances (12).

Genetic susceptibility testing: a paradoxical threat to health protection

If, in spite of their lack of relevance, genetic tests were to be used in recruitment practices in the current context, there is a risk that a situation may arise which from the point of view of health protection at work is paradoxical, for various reasons. Indeed, the idea, and it is often an illusion, that the susceptible individuals are selected out, can lead to a more lax attitude towards prevention in the workplace, with the result that the risk becomes greater for everyone. Moreover, excluding applicants on the basis of genetic susceptibility can lead to *social marginalisation,* with all the negative consequences of it for the health and well-being of the persons concerned. It cannot be emphasised strongly enough that the health of an individual cannot simply be based on the presence or absence of one or another inherited risk factor for a certain occupational disease. That would be a 'reductionist' and all too simplistic or limited approach. This misconception may in practice lead to applicants being classified incorrectly as to their fitness for the job and the protection of their health.

Decision making in occupational health

Within the context of health care, the principle of the autonomy of the individual is central to medical ethics. Respect for autonomy implies that no medical acts will be done without the informed consent of the individual concerned. However, this does not mean that any medical practice to which a person has consented is legally and ethically acceptable. Especially in the field of public health such as in occupational health, individual consent cannot be considered a substitute for balancing values, interests, rights and duties of those concerned and for taking decisions about the acceptability of testing practices at the level of society. Within the context of power inequality in the occupational field, a free and voluntary consent may be an illusion. Contractual freedom between parties increases the autonomy of the stronger (usually the employer) and hampers *de facto* the autonomy of the weaker partner (usually the employee).

If decision making on the acceptability of genetic practices in occupational health would solely be based on the respect for the decisional autonomy principle, practices might be directed by individual stakes and

interests that may conflict with the interest of other workers and applicants, of the work force as a whole, and that make abstraction of the solidarity principle; by the commercial exploitation of new technologies which may set other conditions and goals than the benefit of the individual worker, especially of the more sensitive worker, and of the workforce as a whole; by 'faulty logics' by parties involved, due to simplification of very complex issues which may lead to incorrect deterministic thinking and subsequently to gaps in workers' health protection.

If equity is the aim, decision making in occupational health should primarily be the responsibility of the legislator, who should aim at increasing levers for social protection. The legislator should base his initiatives on social consensus following a thoroughly conducted process of democratic participation after adequate social consultation about the acceptability of practices. The main criterium should be the scientific and practical relevance of the test to the benefit of the individual worker and the working population at large.

The relevance of a test for occupational medical surveillance can best be assessed by the discipline of occupational medicine. Its particular competence consists in trying to establish in as concrete a manner as possible the relationship between specific working conditions and the possible risk to health for a particular individual. Therefore, it can be assessed whether for people with a certain genetic characteristic there is a particular and pronounced risk to health, connected with a certain type of exposure.

In order to allow a correct assessment in the area of occupational medicine, at least two conditions have to be met (10):

(1) Very reliable scientific information has to be available. This is only possible if the means available for impartial scientific research offset the means of possibly biased research, which serves mainly the marketing and commercialisation of genetic tests. Sufficient impartial scientific research capacity on genetic susceptibility should provide the scientific foundations for a policy steered towards social protection and which would prevent the abuse or misuse of genetic susceptibility tests based on prejudice or commercial interests.
(2) There have to be guarantees that the decision serves only the protection of the health of those concerned. These guarantees are connected with the legal aims and mandates of occupational medicine, its structures, regulations and the deontology of its practitioners, and the quality of the control of, and compliance with the regulations.

Conclusion

Genetic testing constitutes a challenge to ethics in occupational health, because – if used as a selection tool – it may easily stand for ungrounded deterministic thinking leading to social exclusion. The problem is not so much that this new technology is about genes, but that such tests, in spite of their lack of relevance, will be marketed in an uncontrolled way and easily be used by non-professionals. In Belgium, the use of genetic screening tests in occupational health is now subject to a general prohibition by law. The legislator allows exceptions to this general prohibition by Royal Decree approved by the Council of Ministers.

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