4.1 ETHICAL ISSUES OF GENETIC SUSCEPTIBILITY TESTING FOR OCCUPATIONAL DISEASES: OPINIONS OF TRAINEES IN A HIGH-RISK JOB

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International Archives of Occupational and Environmental Health 2013, Vol. 86 (7), pp. 827-36
ABSTRACT

Purpose
Genetic research has opened up possibilities for identification of persons with an increased susceptibility for occupational disease. However, regulations considering the ethical issues that are inevitably associated with the use of genetic tests for susceptibility for occupational diseases are scarce. We investigated whether opinions of an intended stakeholder group, that is, student nurses, are sufficiently addressed by existing recommendations.

Methods
Attitudes and opinions of Dutch student nurses toward a genetic test for susceptibility to occupational contact eczema were studied in a qualitative setup using focus groups, interviews and electronic questionnaires. The results were compared with guidelines and recommendations extracted from the literature.

Results
Sixty-nine percent of the student nurses said they would partake in a genetic test for susceptibility to occupational contact eczema when available. Concerns were expressed regarding the difficulty of interpreting test results, the utility of the test result in practice and the necessity of genetic tests for non-severe diseases. For the issue of privacy and confidentiality, the students expressed few worries and much confidence. The existing guidelines largely covered the students’ opinions. Still, the data emphasized the need for good individual risk communication both before and after testing, taking into account that the test concerns susceptibility.

Conclusions
Comparing the students’ statements with the issues addressed by the guidelines, we conclude that the guidelines should pay more attention to risk communication and practical advice accompanying the test results.
INTRODUCTION

Due to recent developments in genetic sciences, opportunities for identification of persons with a genetically determined increased susceptibility to occupational exposure have appreciably expanded. Genetic tests are increasingly accessible, for doctors, companies and the public. The increasing tendency to claim a “right to know”, connected to a strong societal and political emphasis on individual responsibility for health, may further contribute to the demand for genetic susceptibility tests. Detection of susceptible persons at the workplace can improve prevention of occupational diseases, for example, through career counselling or timely application of personal protective measures. However, before actually offering and applying susceptibility tests for occupational diseases, several ethical issues need to be considered. Protective legislation addressing these ethical issues nevertheless is scarce. In 2008, the Dutch Council for Public Health and Healthcare reported that Dutch citizens are insufficiently protected against possible misuse of genetic test results. In the USA workers are protected by the Genetic Information Nondiscrimination Act (GINA), in effect since 2009, which restricts the disclosure of genetic test results to employers and forbids genetic screening in the workplace. European countries lack such legislation, except for Belgium, Finland and Austria, where the use of genetic screening in the work setting is forbidden.

Several guidelines and criteria for genetic screening have been formulated by different committees in Europe, some also focusing on its use in the workplace. Most of these build on the authoritative World Health Organization (WHO) criteria for screening tests for early detection of disease as formulated by Wilson & Jungner. Box 1 summarizes three different guidelines and recommendations on genetic testing for diseases in the workplace that have been published in the last decade. In 2002, MacDonald & Williams formulated six conditions that should be met before offering genetic testing to employees. One year later, the European Group on Ethics in Science and New Technologies (EGE) offered partly similar criteria for acceptability of genetic testing in the workplace. Both sets of criteria concern genetic testing for a variety of diseases, not exclusively those diseases caused by occupational exposure. In a 2006 report on the ethics of genetic screening in general, the British Nuffield Council stated that screening for occupational diseases should be contemplated only when certain conditions are fulfilled. An extensive decision framework for genetic screening tests with 44 questions has been published in 2005 by the Office of Public Health Genomics of the US Centers for Disease Control and Prevention, addressing analytical validity, clinical validity, clinical utility and ethical issues: the “ACCE framework.”

The guidelines and recommendations mentioned above contain many valuable elements; however, for tests that concern susceptibility, some specific aspects need to be considered, for example, the complexity of estimating predictive value. Furthermore, more insight into the attitude of intended examinees in the scenario of tests for occupational diseases would be valuable, but to our knowledge, the number of studies addressing this topic is small.
The objective of this study was to make an inventory of opinions of student nurses regarding a genetic susceptibility test for occupational contact eczema. Further, we investigated whether these opinions are sufficiently addressed by existing recommendations.

Occupational contact eczema (OCE) is one of the most prevalent occupational diseases in western countries\(^1\)\(^4\)\(^1\)\(^5\). It can be caused by an allergic reaction or by mechanical or chemical irritation of the skin. Wet work, involving frequent contact with water and mild irritants such as soap, is a major cause of OCE mostly manifesting as hand eczema. Apart from exposure, individual susceptibility plays a significant role\(^1\)\(^6\). A well-known personal susceptibility factor is atopic dermatitis, an eczematous skin condition which is highly dependent on genetic predisposition\(^1\)\(^7\)\(^1\)\(^8\). Recent research has identified loss-of-function mutations in the filaggrin gene (\(FLG\)) as a major risk factor for atopic dermatitis\(^1\)\(^9\). Furthermore, these mutations are suspected to increase the risk of developing contact eczema as well\(^2\)\(^0\)-\(^2\)\(^3\). In a recent case-control study, significant associations were found between OCE and atopic dermatitis and between OCE and \(FLG\) loss-of-function mutations with odds ratios of 2.89 and 1.61, respectively. Combined presence of \(FLG\) mutations and atopic dermatitis increased the risk of OCE approximately fivefold (Visser et al., in preparation). In Germany and in the Netherlands, nurses, being at risk for developing OCE due to frequent wet work, are presently screened for increased susceptibility to develop OCE using history of atopic dermatitis as an indicator. Susceptible individuals receive extra preventive measures and are regularly followed-up by their occupational physician\(^2\)\(^4\)\(^2\)\(^5\). Possibly, \(FLG\) genotyping could improve the evaluation of susceptibility to OCE.

METHODS

Students in training to become a nurse were recruited from three schools for higher or intermediate vocational education, all located in Amsterdam, the Netherlands. The school institutional review boards agreed with the study protocol.

A detailed description of the recruitment process and data collection methods is presented elsewhere\(^2\)\(^6\). In short, a literature search was performed to identify factors that could influence decisions, beliefs or attitudes towards the use of genetic susceptibility tests. This resulted in a list of factors clustered in nine themes: “Emotions”, “Expected effects of the disease”, “Risk of developing the disease”, “Expected use of test results”, “Confidentiality and privacy”, “Personal involvement” (e.g., having had the disease yourself, or knowing someone who has), “Social influences” (e.g., by family members, colleagues, media), “Principles and beliefs” (e.g., religious beliefs) and “Practical issues”. Factors regarding test content were classified under the themes “Expected use of test results” and “Practical issues”.

Consecutively, students were invited to voluntarily participate in a focus group, interview or electronic questionnaire, whichever involvement method they preferred.
Different recruiting techniques were used: a sample of student nurses participating in an ongoing cohort study (Visser et al., in preparation) and studying in the Amsterdam area were invited by email. Posters were placed on school message boards and in cafeterias, and students were approached directly by 2-minute oral presentations in classes or in central study areas. During 2009/2010 a total of 5 focus groups (each 5–8 participants; a total of 33 participants) and 15 semi-structured interviews were held with student nurses. In addition, 32 students filled in an electronic questionnaire. The total number of participants was 80. Each student participated in only one involvement method. The percentage females was 80%, and the mean age was 23 years (range: 17–45). The distribution of respondents over the first to the fourth educational year was 18, 19, 32 and 32%, respectively.

Focus groups, interviews and electronic questionnaires were set up following a similar standardized protocol. First, a brief introduction was given to the students about OCE (“hand eczema”), skin exposure and protection, and personal susceptibility. Subsequently, the possibility of testing personal susceptibility with a genetic test was introduced followed by two questions: Question 1. “Would you use this test?” (possible answers: yes/ no/ doubt) and Question 2. “What are your motives for using or not using this test (according to you, what are the pros, cons and doubts)?” (open question). After all pros, cons and doubts brought up by the participants had been recorded, in all involvement methods the list with the factors extracted from the literature was introduced, clustered by theme. Respondents were asked whether (yes or no) and how or why (open question) these factors would influence their choice whether or not to use the test, and which (if any) other influential factors they could think of within the theme in question. Finally, after all themes had been discussed, participants individually prioritized which three themes they regarded as most important and which three themes they regarded least important.

RESULTS

In total, 55 out of 80 student nurses (69%) stated that they would take a genetic test for susceptibility to OCE if such a test was available. Eleven students (14%) stated they would not take such a test, and 14 (18%) doubted if they would take it or not.

The aim of this study was to identify the most relevant arguments in favor or against using the test expressed by the student nurses. Due to the character of the focus groups, which yielded data on group level instead of the individual level, the resulting opinions could not be referred to (numbers of) individual participants. Therefore, no information on the exact proportion of respondents that mentioned a certain opinion can be given. The arguments that were brought up will be reported below in a qualitative manner, clustered by theme.

At the end of the focus groups, interviews and questionnaire, the participants were asked to mark the three themes they considered most important and three themes they considered least important. Participants in the focus groups wrote their
Box 1. Three examples of existing recommendations and guidelines addressing genetic screening in the workplace

**Criteria for offering genetic testing to employees, according to MacDonald & Williams-Jones (2002)**

- A genetic test (for a specific condition) must be available which is highly specific and offers an acceptably low incidence of both false positives and false negatives; such a test must test for a gene that is sufficiently penetrant for the test result to have some important health implication.
- Testing should be carried out by an independent lab, and results of genetic tests should be given to workers directly, either by a geneticist or a genetic counselor; test results should be held confidential, and revealed to the employer only at the employee's request.
- Pre- and post-test genetic counseling must be available from a qualified health professional, and paid for by the employer, regardless of the outcome of the test.
- The gene being tested for must not be prominently associated with an identifiable and historically disadvantaged group.
- Where relevant, the employer must guarantee continued access to group insurance.
- The employer must ensure that if the employee chooses to reveal that she has tested positive, suitable policies are in place to ensure a reasonable degree of job security.

**Conditions that must be fulfilled before genetic screening at the workplace can be considered, according to the European Group on Ethics in Science and New Technologies (EGE) (2003)**

- The performance of the test is necessary for guaranteeing the protection of the employee's health and safety or those of third parties.
- The applicant or the employee should consent to the genetic test.
- There is scientifically proved evidence that the genetic test is valid and is the only method to obtain this information.
- The performance of the test does not prejudice the aim of improving conditions in the workplace.
- The principle of proportionality is respected regarding the motivations involved to perform the test.
- The principle of non-discrimination is not violated.
- The applicant or the employee should receive full information from an independent health professional on the testing procedure, the reasons for performing such tests, the potential outcomes and their implications and consequences, as well as the conditions of storing and access to data. They should also, if requested, be provided with access to independent legal counselling.

**Conditions for genetic screening of employees for increased occupational risks, according to the British Nuffield Council on Bioethics (2006)**

- There is strong evidence of a clear connection between the working environment and the development of the condition for which the screening is conducted.
- The condition in question is one which seriously endangers the health of the employee or is one in which an affected employee is likely to present a serious danger to third parties.
- The condition is one for which the dangers cannot be eliminated or significantly reduced by reasonable measures taken by the employer to modify or respond to the environmental risks.
prioritization on a separate sheet of paper, so that for this subject individual results could be obtained. Table 1 lists the themes with their relative importance given by 70 out of 80 students (10 questionnaire respondents declined to prioritize the themes). Some illustrative quotes are shown in Table 2.

**Emotions (e.g., curiosity or anxiety)**

The theme “Emotions”, including curiosity and anxiety, was rated as important by many students in their prioritization of themes, especially by those who were in favor of partaking in the test. Several participants stated they were curious about their personal susceptibility, and would like to use the test to find out, or, in some cases, to confirm their own suspicions about their personal susceptibility (e.g., someone who already had contact dermatitis, or someone with a dark skin tone suspecting to be less susceptible). Also, knowledge of personal susceptibility would provide some kind of comfort. In contrast, a number of participants feared that the test would only lead to uncertainty and nervousness about developing OCE, especially in the case of a positive test result. They would rather not suffer from this stress, and instead just “wait and see”.

<table>
<thead>
<tr>
<th>Theme</th>
<th>% of respondents (n = 70) scoring this item as</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Important</td>
</tr>
<tr>
<td>Expected use of the test results</td>
<td>56</td>
</tr>
<tr>
<td>Expected effects of OCE</td>
<td>54</td>
</tr>
<tr>
<td>Emotions</td>
<td>50</td>
</tr>
<tr>
<td>Risk of developing OCE</td>
<td>40</td>
</tr>
<tr>
<td>Confidentiality and privacy</td>
<td>24</td>
</tr>
<tr>
<td>Personal involvement</td>
<td>21</td>
</tr>
<tr>
<td>Practical issues</td>
<td>20</td>
</tr>
<tr>
<td>Social influences</td>
<td>14</td>
</tr>
<tr>
<td>Principles and beliefs</td>
<td>4</td>
</tr>
</tbody>
</table>

**Expected effects of the disease**

The effect that OCE would have on work and private life was also a highly prioritized theme for those who were in favor of testing. These students stated that in addition to impaired work functioning for the affected person, for example, due to sensitive skin and pain, OCE may also lead to decreased hand hygiene compliance. This relates to the fact that most hand hygiene products, like disinfectant or alcohol gel, can be
Table 2. Arguments in favor of or against partaking in a genetic test for susceptibility to occupational contact eczema, expressed by student nurses

<table>
<thead>
<tr>
<th>Theme</th>
<th>Illustrative argument(s):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotions (e.g. curiosity, anxiety)</td>
<td>[+] “I would rather be afraid of something I know, than of something that is uncertain. I want certainty”.</td>
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<tr>
<td></td>
<td>[+] “Everything you know is a bonus, everything you don’t know is a lack of knowledge”.</td>
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<tr>
<td></td>
<td>[+] “I am curious: I want to know what eczema is, where it comes from, and what the consequences are”.</td>
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<tr>
<td></td>
<td>[-] “Life would be really boring if you already know what’s going to happen”</td>
</tr>
<tr>
<td></td>
<td>[-] “I can’t cope with that, you’ll keep worrying: when does it start, when will it happen to you! That uncertainty is terrible”.</td>
</tr>
<tr>
<td>Seriousness of the disease</td>
<td>[+] “I would be ashamed if I suffered from serious hand eczema, that attracts attention, people will think you are dirty”.</td>
</tr>
<tr>
<td></td>
<td>[+] “If you don’t feel well yourself, you cannot give good care”.</td>
</tr>
<tr>
<td></td>
<td>[-] “In general, hand eczema is not awful. It’s a bit of a small issue. To screen everyone in the nursing profession is nonsense”.</td>
</tr>
<tr>
<td>Expected use of the test results</td>
<td>[+] “I can use the test outcome to take extra preventive measures, wear gloves, use more hand cream. And there are plenty good preventive means”.</td>
</tr>
<tr>
<td></td>
<td>[-] “In principle, you are responsible [for preventing OCE] both before and after testing, and then I wonder: to what extend will the test make that responsibility grow, or decrease? I think the responsibility is your own anyway, and not with a test”</td>
</tr>
<tr>
<td></td>
<td>[-] “When you see the first symptoms of hand eczema, you can always start to be more careful then, by using extra lotions etc.”</td>
</tr>
<tr>
<td></td>
<td>[-] “I know there are preventive measures, but it’s not enough for me. How can I be sure that I don’t get it, if I take the preventive measures? It’s not like a pill, you have to pay so much attention all the time”.</td>
</tr>
<tr>
<td></td>
<td>[-] “I have doubts about the effectiveness of preventive measures. For example, using cotton gloves underneath other gloves, isn’t that just too much effort and a waste of money?”</td>
</tr>
<tr>
<td>Risk of developing OCE</td>
<td>[+] “There is no certainty, but the risk is that high so I would want to know”.</td>
</tr>
<tr>
<td></td>
<td>[-] “If hand eczema would be very prevalent, I would be more willing to take the test”.</td>
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<tr>
<td></td>
<td>[-] “Even if the risk would be 1 in 2, I still think, if you never had any trouble with your skin, then I think the chance is lower to develop it eventually”.</td>
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<tr>
<td></td>
<td>[-] “1 out of 5 nurses develops hand eczema, so the chance is 1 out of 5 that that would be me, and if my risk is increased, the chance would only be higher that I would be that 1 out of 5. But 1 out of 5 already is quite a high chance. So that doesn’t say very much”.</td>
</tr>
<tr>
<td></td>
<td>[-] “If you have an increased risk, I wouldn’t put at stake the profession that you like to practice because perhaps you will get hand eczema”.</td>
</tr>
<tr>
<td>Confidentiality and privacy</td>
<td>[-] “It should be well protected, especially with genetic information, because that not only concerns yourself but also your family”.</td>
</tr>
<tr>
<td></td>
<td>[-] “I am afraid that my DNA would be used for other tests without my permission”.</td>
</tr>
<tr>
<td></td>
<td>[-] “Nobody else should know my genetic makeup. It could be used against you, so it is important that this information is not accessible for others ”.</td>
</tr>
<tr>
<td></td>
<td>[+] “I really don’t get why people are so scared about preserving their privacy, for example with the issue of electronic patient records. […] There is just the duty of professional confidentiality, and I assume that everyone who has access to the test results) keeps to that”.</td>
</tr>
<tr>
<td></td>
<td>[+] “If you provide a DNA sample in a hospital, what can possibly go wrong?”</td>
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<tr>
<td></td>
<td>[+] “I could use the test results as a kind of “proof” for my manager, in order to claim extra preventive measures, e.g. gloves, creams, soap. But not without my permission”.</td>
</tr>
</tbody>
</table>
painful when applied on damaged skin. Furthermore, colleagues would have to work extra shifts because of sick leave of the affected person. Because of their professional involvement, students felt responsible to maintain a healthy skin to be able to perform their work according to hygiene standards. They also mentioned that patients may not want to be treated by a nurse with hand eczema, because they think it is “dirty” or even infectious. As hand eczema is a disease that is directly visible and “cannot be hidden”, these participants acknowledged a high impact of this condition in the social field. Other participants, however, thought that OCE is a non-severe, easy treatable disorder (“hand eczema is not cancer”) and considered it to be “not serious enough to test for”.

### Expected use of the test results

The expected utility of the test results was prioritized as important by many participants who were in favor of testing, but it was also the theme with the highest prioritization rating for those who stated they did not want to be tested or for those who doubted. Participants who were in favor of testing said that knowledge of their susceptibility would motivate them to practice better skin care and avoid exposure where possible. On the other hand, some stated that skin care and preventive measures should be taken by everybody, not only by susceptible persons, and that a test therefore would have no added value. Taking protective measures was seen as “your own responsibility”; however, as this was used as an argument against testing by some participants, others used it as an argument in favor of testing.

Some participants expressed the concern that a positive test result might lead to over-protective behavior and “hypochondria”, which would jeopardize the compliance to hand hygiene, or in the opposite case that people who find out to be not susceptible would become careless about their skin care and exposure or ignore the first symptoms of OCE leading to a delay in seeking treatment. Less than 10% of the participants mentioned that they would use the test results as an advisory component in their choice of professional training or career prospective.

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**Table 2. Arguments in favor of or against partaking in a genetic test for susceptibility to occupational contact eczema, expressed by student nurses (continued)**

<table>
<thead>
<tr>
<th>Theme and other considerations</th>
<th>Illustrative argument(s):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principles and other considerations</td>
<td>[-] “The end is lost; you may scan for anything these days”.</td>
</tr>
<tr>
<td></td>
<td>[?] “I worry that genetic research would make life manipulable and predictable. I can see the necessity of genetic research for serious illnesses, but shouldn’t we draw a line somewhere?”</td>
</tr>
<tr>
<td></td>
<td>[?] “People always want to have more information, but you never think about it beforehand what it does to you. You should think about it before you do the test, because afterwards, you cannot go back”</td>
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</tbody>
</table>

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**ETHICAL ISSUES OF GENETIC SUSCEPTIBILITY TESTING FOR OCCUPATIONAL DISEASES**

4
Risk of developing OCE

The fact that a positive test result does not mean that a person will develop OCE with certainty and, the other way round, a negative test result is no guarantee for not developing OCE was considered a significant disadvantage. For this reason, a number of participants thought that undergoing a susceptibility test was pointless. At the presenting of the case, the students were told that the chance of acquiring OCE during an average nursing career is about 20%, or 1 out of 5, and that taking the test would inform you whether your personal risk would be higher or lower than 1 out of 5. This led to a diversity of reactions, such as

“On average 1 in 5, so, the chance that you get it is smaller than the chance that you don’t get it”,

“Considering how often we have to wash or disinfect our hands, I’m surprised that the probability is not higher”,

or

“I think that is a lot, I had expected something like 1 out of 100”.

Although the majority of the participants thought a prevalence of 20% was high, some regarded this as an argument against taking a test, because “the risk is high anyway”. Nevertheless, others stated that information on an increased risk would still be relevant for them, even more so if that risk was high to begin with. Although many students acknowledged that they had difficulties interpreting the risk to develop OCE, the height of the risk was still a reasonably important factor in their considerations whether or not to take the test.

Confidentiality and privacy

A few participants emphasized the importance of protecting confidentiality of genetic test results; however, in general, questions about privacy and protection of personal test results were a relatively minor issue in the students’ considerations. When specifically asked about it, most participants stated that they felt confident that such matters would be appropriately taken care of. Some thought that society’s worries about privacy are exaggerated, referring to their experience that, at least in the medical setting, confidentiality is generally secured by the “oath of secrecy”. Regarding the question of which (if any) parties should be allowed access to the test results, the majority allowed researchers and their general practitioner access to the test results and considered access by employers and insurance companies as unacceptable. However, some participants stated that disclosure of test results to employers also may have a positive effect: the employer could be convinced to supply personal protective equipment and skin care products. Disclosure of results to family members was a point of doubt, because on the one hand, they may benefit from this knowledge in view of preventive measures (this also applied to future offspring), but on the other hand, one may not want to raise unnecessary concern.
**Personal involvement, Social influences, Principles and beliefs, Practical issues**

Participants who had personal experience with hand eczema themselves, or had close relatives with hand eczema, were more inclined to take the test. This did not apply for participants who had seen the disease in friends or colleagues. The opinion of friends, colleagues and family members, or other social influence by, for example, school teachers, professional journals or the Internet was not regarded as influential by most participants. Nor was religion; only one respondent stated that she would not take the test because of religious constrains, while several other respondents who professed a religion said that taking a medical test would not interfere with their religious beliefs.

A few participants expressed fundamental doubts about testing for OCE susceptibility, of which most thoughts were in the line of OCE being not “serious” enough to justify testing, or in the line of “what’s next?” and “should we really want to know everything?”.

As the case presented to the students was about a hypothetical test, practical issues like the logistics of the test method (e.g., self-test or clinical setting) and costs were not mentioned initially. When this theme was addressed by the researchers it was acknowledged to be influential but not decisive for their considerations.

**DISCUSSION**

Sixty-nine percent of the student nurses stated that they would agree to be tested for susceptibility to OCE. The most important arguments in favour of testing were curiosity and the possibility for preventive measures. On the other hand, concerns were expressed regarding the difficulty of interpreting test results, the utility of the test result in practice, and the usefulness of genetic tests for less serious diseases.

Most of the opinions expressed by the students are addressed in existing guidelines. In addition, many students mentioned the difficulty of risk interpretation and the need for practical advice accompanying the test results, elements that are hardly elaborated in the guidelines we reviewed. We will discuss the students’ opinions in the light of existing guidelines, according to the themes mentioned before and in the order we consider as most appropriate to follow when choosing to offer a susceptibility test or not. Finally we will also briefly discuss test validity, which is an important condition, but was not a subject for the student nurses study.

**Seriousness of the disease**

Some of our students questioned if OCE is serious enough to test for. This corresponds to “seriousness of the disease” mentioned in all existing guidelines. Adverse effects on work performance and effects on quality of life should also be considered here. In the scenario of career counseling, milder diseases can be accepted as precondition to allow the offering of susceptibility testing than in the scenario of a pre-employment examination where selection of workers may be the consequence.
Expected use of the test result and possibilities for preventive measures

Most of the thoughts on utilizing the test results to take preventive measures expressed by the students were related to means of exposure reduction in the workplace. The remark of several student nurses that protective measures should be taken by everyone, regardless of susceptibility, corresponds with the view expressed by several authors that susceptibility testing should not shift the focus from exposure reduction in the workplace to selection of individual workers \(^{2,3,7,27-29}\). Measures to reduce exposure on workplace level always come first, following the so called occupational hygiene strategy.

Effective preventive measures must be available for those who test “susceptible”, for example extra personal protective equipment and an educational program or a change of work tasks. However, even if preventive measures are available, they may not be recognized as an argument in favor of testing by (part of) the target group. Some of the students stated that they would not change their skin protection behavior anyway. Two earlier studies investigating the willingness to take a genetic test among young adults have found similar results. Harel et al. (2003) used a questionnaire survey among 361 high school students (16-18 years) to assess whether or not they would be interested to take a genetic test for hypercholesterolemia, for breast cancer and for Tay Sachs disease \(^{30}\). One of the most important arguments against testing for hypercholesterolemia was “I would not act on the results anyway”. In a recent interview study among 33 American college students, only one-third of the participants stated that they would be interested in taking a genetic test for susceptibility to lung cancer and that they considered a “positive” result as an extra motivation to quit smoking \(^{31}\).

Interpretation of risks and communication of test results

The difficulty of risk interpretation and the need for practical advice accompanying the test results is lacking in most recommendations about genetic testing for occupational diseases. MacDonald & Williams-Jones recommend genetic counselling, but do not specify which components this counselling should include. Risk interpretation is difficult, especially for susceptibility tests as these only provide a change in probability to develop a disease. Even if risk information is well communicated, the individual’s interpretation of personal risk may be confused by non-rational lines of reasoning, such as “binary thinking”, where people perceive any risk – regardless of its actual size – in a binary (yes/no), not a graduated (probabilistic) way \(^{32,33}\). The European Group on Ethics expressed that researchers, policy makers and companies implementing susceptibility tests should beware of misinterpretation of risk estimates too \(^4\). Furthermore, perception of risk is known to be dependent on personal context, including emotions, and people may exaggerate or downplay risks regardless of the numerical probability they assigned to it \(^{33,34}\). The influence of subjective values and emotions on risk interpretation should not be underestimated. Adding practical
advices to the test results will promote adequate behaviour and may help to prevent, for example, hypochondria and the “carte blanche effect”\textsuperscript{2,7,35}.

**Voluntary consent**

It was mentioned by several student nurses that the test should be offered on a voluntary base and that it should be up to the tested individual to disclose the results to their employer or not. It can be questioned, however, to what extent genuine voluntary testing can be achieved in a workplace setting \textsuperscript{2,3,29}. Workers may fear that refusing to take the test may have negative consequences for their position. The employer should ensure that participation is voluntary and that there are no consequences for those who refuse to be tested. Preferably, the test should be executed by an independent organization, so that feelings of mistrust among workers are prevented.

**Confidentiality and privacy**

Worries about privacy and confidentiality were expressed by only a few student nurses; many respondents stated that they were confident that such matters would be properly taken care of. Furthermore, whereas most ethicists are worried that employers may abuse test results for employee selection, a few of our participants came up with the idea of using a positive test result to convince employers to supply extra protection. The confidence in privacy protection may reflect the optimistic views of a relatively young population that has not (yet) experienced situations where privacy may be violated. Similarly, in the study of Harel \textit{et al.} (2003)\textsuperscript{30} only a quarter of the students agreed with the statement “I am worried that results will be misused by my insurance company / employer”. In contrast, privacy and confidentiality issues were the main concerns expressed in three recent American surveys, i.e. among beryllium workers and their relatives\textsuperscript{13}, employees of a university research centre and a national laboratory\textsuperscript{12} and unionized workers\textsuperscript{36}. The workers in the study of Brandt-Rauf \textit{et al.} (2011)\textsuperscript{36} distrusted even their own physicians, despite their oath of secrecy. The fact that most occupational physicians have to protect the workers as well as the interests of the companies they work for often gives rise to a suspicious attitude among workers towards their occupational physicians\textsuperscript{37}. The arrangement of privacy and confidentiality issues, including who has access to the results, should be clearly communicated in the test information.

**Test validity**

In our study of the student’s opinions, the validity of the test was not a subject for investigation. However, because of the specific character of genetic susceptibility tests, the test validity—in the widest sense—deserves attention.

Analytical validity (reliability) for genetic tests will approach 100%. The clinical validity of susceptibility tests, however, is difficult to assess. For presymptomatic tests of present disease, the error can be expressed relatively simple by the “predictive”
value of a positive or negative test result. For susceptibility tests, the error in the prediction of future disease is more complex, as it contains unknown elements that often cannot be assessed: the extent of future exposure, the presence of non-tested susceptibility or protection factors, and interactions between these factors, including the tested gene. This holds especially for predicting the disease risk for an individual.

Nevertheless, before offering a test one should estimate, using some assumptions, the predictive values on group level. For example, if in a group of 100 workers the frequency of the susceptibility gene is 10%, the relative risk of acquiring the disease in carriers of the susceptibility gene versus non-carriers is 3, and the lifetime incidence of the disease at the prevailing level of exposure is 20% for the whole group, the probability of developing disease in carriers and non-carriers can be calculated as 50% (5/10) and 17% (15/90), respectively, see Table 3.

As the incidence of occupational diseases depends on the extent of exposure and on the presence of not tested susceptibility factors, the probability of disease can be estimated from data stemming from another population only with due consideration of these factors. This should be considered for every new application. Furthermore, in this example 50% of the carriers will not develop disease while 17% of non-carriers will still develop disease. The importance of the 50% healthy positives and 17% diseased negatives should be considered (in tests of presymptomatic disease the corresponding groups would be called false-positives and false-negatives; however in susceptibility testing there is no such “false”). Healthy positives may experience unnecessary worry or even unjust exclusion from jobs. Diseased negatives would also have occurred without testing; their presence points to a low efficiency of the execution of the test in this population, that is, they limit the preventable fraction.

The practical consequences of the presence of healthy positives or diseased negatives will differ depending on the type of disease, the characteristics of the target population and available treatment or prevention options with different kinds of benefits and harms. In the case of a susceptibility test for hand eczema, for example, a healthy person with a “susceptible” test result would receive unneeded extra skin care resulting in unnecessary costs, whereas a person who would falsely test “non-susceptible” would receive only standard skin care where extra skin care would be needed. In this case, the consequences of being a “diseased negative” could be more serious than that of being a “healthy positive”. For tests for diseases requiring invasive treatment or complete elimination of exposure (which could result in job loss) this can be the other way round.

This study presented opinions concerning ethical aspects of the use of a genetic susceptibility test for OCE among student nurses. As our participants were recruited by convenience sampling in a single city, the results cannot be extrapolated to other populations without considerations. Nevertheless, we confirmed that most opinions expressed by a student nurse stakeholder group as described are covered by the existing guidelines on genetic testing in the workplace.
Comparing the students’ statements with the issues addressed by the guidelines, we conclude that the guidelines should pay more attention to risk communication and practical advice accompanying the test results. In our opinion, the following key elements should be considered for the choice to offer a test or not: (1) validity of the test, including analytical reliability, frequency of the trait, relative disease risk of the trait, and expected disease frequency, (2) the seriousness of the disease, and (3) the possibilities for prevention and related benefits and harms. Three additional elements related to the implementation of the test should be considered: (4) risk communication and need for practical advice accompanying the test results, (5) voluntary consent and (6) privacy and confidentiality. Guideline development can be organized by public health officials, associations of occupational physicians or other occupational health care providers. Our data emphasize the need for good individual risk communication both before and after testing, taking into account that the test concerns susceptibility.

ACKNOWLEDGEMENTS

We are grateful to the participating student nurses and the Hogeschool van Amsterdam, ROC ASA and ROC van Amsterdam for their cooperation in this study. We also thank the Foundation Institute GAK (Hilversum, the Netherlands) for funding this study.

REFERENCES


Table 3. Frequency of occupational disease depending on the presence of a susceptibility trait

<table>
<thead>
<tr>
<th>Susceptibility trait</th>
<th>Disease will develop (at continuing exposure)</th>
<th>Disease will not develop (at continuing exposure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present (“positives”)</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Not present (“negatives”)</td>
<td>15</td>
<td>75</td>
</tr>
<tr>
<td>All</td>
<td>20</td>
<td>80</td>
</tr>
</tbody>
</table>

Example: 100 subjects, carrier frequency = 10%, relative risk of disease = 3, cumulative disease incidence = 20%.


32. Tijmstra TJ, Bajema C. ['You should be that one exception'; risk perception and choice behavior in medical technology]. *Ned Tijdschr Geneeskd* 1990; 134: 1884-5.


