

## Genetic testing and screening

### Introduction

This activity encourages students to read an article which provides a good overview of the issues involved in genetic testing. It will also teach them useful reading skills, thinking more carefully about the meaning of each section so that they can supply their own headings.

### The activity

We suggest that the students read the article in class and discuss the headings as a whole class activity. The questions can be answered in class or as homework.

### Suggested answers to questions

#### Headings

The headings are not part of the original article but have been included here with the author's permission.

- 1 Screening for PKU
- 2 Why PKU screening works particularly well
- 3 CF screening and its dilemmas
- 4 Screening for late onset conditions
- 5 Risk reduction
- 6 Protection for individuals at risk or for everyone?
- 7 Some principles
- 8 Differing individual reactions

- 2 Screening means that everyone is tested as opposed to only those with symptoms or a family history.
- 3 1:15 000
- 4 The total cost of testing, though not small, is less than the cost of caring for those who would be handicapped if they developed mental retardation because they had not been identified and put on a special diet.
- 5 The test is not 100% accurate, there are false negatives, only 85% of couples identified.  
Dilemma of whether to test the unborn child  
Dilemma of whether to have an abortion if fetus has CF Is CF serious enough to justify abortion, there may be cures in the future
- 6 No treatment or preventive measures and may spoil current life with worry  
Implications for other family members who may also have gene  
Risk of discrimination for insurance or employment
- 7 Too much focus on individuals at high risk may lead to neglect of measures to improve overall health, such as health education.  
Genes are not the only risk factor for heart disease.  
In the workplace identification of those at particular risk of chemical exposure might lead to the neglect of attempts to reduce exposure for all workers.
- 8 Strong motivation to reduce other risk factors  
Example of these risk factors  
Protection of other family members in same way  
Stress of knowing about future health problem  
Risk of discrimination in work place or insurance  
A negative result might make you careless about health

You may wish to use the level based mark scheme used for longer answers in the exam. See the mark scheme for the review question on stem cells in Topic 5 activities.

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### Genetic Testing and Screening; A mixed blessing?

Jon Turney (2002) in 'Understanding Bioethics: De-coding the issues' Reiss and Levinson (eds), Routledge/Falmer

1

If you were born in the UK, you have already been screened for a genetic disease. As in many other countries, a drop of blood is taken from the heel of every newborn baby, and sent off for lab tests. One of the tests - the first to be used, in around 1960 - identifies children who have more than the usual amount of a particular chemical in their blood. Those who have too much of the chemical, phenylalanine, are then looked at more closely.

That is because some of them will have the genetic disorder phenylketonuria (PKU). If they do, their cells cannot make a particular protein, an enzyme, which helps them digest phenylalanine, a component of many proteins. Accumulation of phenylalanine in the body causes mental retardation. But it can be prevented by putting children with PKU on a special diet.

This whole procedure is an example of *screening* because there is no selection of individuals for testing. It is applied, in this case, to the whole population. And most people think this is a good idea. There are drawbacks (there always are). The tests have to be applied carefully to avoid diagnosing PKU in babies who do not have it (false positives in the trade). Putting them on a phenylalanine restricted diet is harmful. For those who do have PKU, the diet is boring and costly. And a girl with PKU who grows up to have children must have a special diet during pregnancy, too.

But, on the whole, PKU testing works. The condition is pretty rare, but it used to cause about one in 100 cases of serious mental retardation. These have now been virtually eliminated. And although 15,000 babies are tested for every one found to have PKU, it still saves money.

You might think, then, that the promise of a whole lot more genetic screening - based on our new, very detailed knowledge of genes and DNA rather than on testing blood chemicals - would be good news. But if we look more closely at the PKU test, we can see why other screening programmes might not be so straightforward to assess.

2

In PKU, a whole set of features come together to make screening successful. It is a simple condition, genetically speaking. Everyone is equally likely to be exposed to the chemical which causes the damage to affected individuals because we all eat it. The test, if properly carried out, is reliable. It is easy to interpret, in the sense that the outcome of untreated PKU is pretty much a certainty. It involves a condition present at birth, but the test is done on the baby, not the parent or the foetus. And there is a relatively simple and effective treatment. Even then, the experience of PKU testing has revealed some pitfalls as well as great benefits, as historian Diane Paul points out. (Paul, 2000). Few other tests exhibit all these features, and varying any one of them makes it much harder to decide whether screening is a good idea.

3

To see how, let's look at the slightly more complicated case of cystic fibrosis (CF). This is caused by a gene which occurs in altered form in about one white person in 20. They are healthy carriers, as their other copy of the gene works properly: CF is a recessive disorder. When two carriers have a child, on

average one in four of the children will have two copies of an altered form of the gene, and show signs of the disease. These include sticky mucus in the lungs, which leads to infections, and problems with digestion.

In 1989, the gene involved in CF was identified, and in theory it is now easy to test prospective parents to see if one or both carries an 'unhealthy' gene variant. But the test is not completely reliable. The gene for the protein which does not do its job properly in people with CF, known as CFTR, is a large one, and nearly 1,000 different mutations have now been found in the DNA code. Although many of these are rare, even the best testing now on offer only picks up 85 per cent of couples at risk of having an affected child.

Now put yourself in the position of someone who has tested positive for one of the common alterations in the gene. You can suggest that your partner has the test, too. But if their test is negative, you cannot be *absolutely* sure there is no risk if the two of you have a child. If it is positive, the only way to be sure your child will not have CF is to have another, prenatal, test, using the unborn child's DNA. If that shows that the foetus has two copies of the affected gene, you may choose to have an abortion.

On the other hand, you may have moral objections to abortion. Or you may just be an optimist. CF causes premature death, but it does not induce a profound handicap like PKU. The treatments are not much good, but they are getting better. Life expectancy for people with CF is increasing all the time, though it is still low. There is talk of gene therapy to correct the defect, which might even become possible in your child's lifetime. All this you have to weigh up in making your decision. You may feel that the offer of the genetic test for CF has made your life more complicated, not simpler, more stressful rather than less.

These complexities arise when only a few of the features which made PKU simple to think about were changed. Cystic Fibrosis is still a relatively simple condition. Only one gene is involved, and the probability that you will have the disease if you are born with two altered copies of the gene is very high (though not 100 per cent, and the severity of the symptoms varies).

#### 4

Other screening tests likely to be on offer in future will differ in other ways from PKU. Two extremely important differences are that they will more often involve conditions which affect people later in life - 'late onset' disorders - and they will concern illnesses influenced by many different things - multifactorial conditions. There are many risk factors for heart disease, for instance, including fatty diets, lack of exercise, and smoking. Will we regard having a few dodgy genes as just another risk factor, or will they seem specially important, *because* they are genes? Similar questions arise for many forms of cancer. The third complication to note is that new technologies, like so-called 'gene chips', are likely to make it easy to screen for many genes at once.

What does this mean? The result of a single screening test will not mean that you have a problem (or are free of it), and will not mean that if you have it you have it now. It will mean that you might be susceptible, you may be more at risk, something unpleasant may happen to you, one day. Then again, it might not. Now what do you do?

For example, we know that one of several proteins involved in blood transport of the fatty chemicals called lipids, apolipoproteinE, occurs in three different versions. If you have two copies of the gene for APOE4, and seven per cent of people in Europe do, you have a ninety per cent chance of getting Alzheimer's disease when you are older. Worse, the devastating symptoms of Alzheimer's like loss of memory and, ultimately, identity, are likely to begin in your late sixties instead of, as in the majority of cases, in your eighties.

But why would you want to know? There is, as yet, no treatment, and no real idea how to prevent the disease. Will it help you to be told, if you know the disease has cropped up in your family, that you

yourself are at high or low risk? Most doctors and ethicists doubt that it will (Post et al 1997). And who else are you going to tell, and when?

A case like this also raises other problems. Does a doctor who gets a result from such a test have any obligation to other members of the patient's family? Do insurance companies have any right to ask about such a test? If they do not, what is to stop someone who has tested positive from buying loads of extra life insurance? Would it be helpful to have granny tested before taking out a mortgage on that house with the downstairs flat attached so you can keep an eye on her as she grows older? One writer has wondered what would have happened if someone had tested some of the already elderly Ronald Reagan's cells for the DNA signature of Alzheimer's when he was running for US president (Ridley, 1999). We certainly know that he came down with the disease soon after he left the White House.

**5** \_\_\_\_\_  
This is not to say that susceptibility tests like this may not bring benefits. The same apolipoprotein genes, for instance, are implicated in heart disease, and people with particularly risky combinations can watch their diet. As Ridley puts it, "the medical profession must soon learn to seek which of us could profit from such a warning and which of us can relax and hit the ice cream". But this perhaps suggests a clear cut difference between risk categories which may not often appear.

It also assumes a rather simple response to warnings about risk. But such responses tend to be anything but simple. Research suggests that people's reactions to being told they may face a genetic risk can range from denial - "it won't happen to me" - to fatalism - "I'm going to get it anyway, so there's nothing I can do". Neither response produces the preventive response which would actually help some people.

**6** \_\_\_\_\_  
Mention of prevention also points to another, broader concern. If medicine comes to focus on identifying people at higher risk of common conditions like heart disease or cancers, will that discourage more general preventative efforts, whether based on health education or, say, alleviating the poverty which may make it harder to maintain a healthy diet?

A particularly acute form of this dilemma can arise in the workplace. For instance, the metal beryllium is essential for making nuclear weapons, among other things, but exposure to even small quantities can lead to chronic beryllium disease, a serious or even fatal lung condition. Employers, such as the Los Alamos National Laboratory in the US, try and reduce exposure to beryllium, but cannot eliminate it completely. Recently, genetic markers have been found which indicate an unusually high sensitivity to beryllium. Should the laboratory test for these, and advise those who test positive to move to different jobs? Or will this reduce the incentive to cut beryllium exposure for everyone else, or to monitor all workers for early signs of the disease? At the time of writing, Los Alamos is "considering how it might implement a voluntary genetic testing programme that would provide private information to beryllium workers about their genetic risk", according to the laboratory.

**7** \_\_\_\_\_  
As this suggests, there are principles which may guide use of new tests in ways which help maximise the benefits and minimise problems. They need to go beyond simple cost-benefit analyses sometimes favoured by health planners and decision-makers. If a test is voluntary, as the Los Alamos approach suggests, then it is usually suggested this must mean some kind of *informed consent*.

This can itself be quite complicated to think through. As the British Nuffield Council on Bioethics put it, "consent to screening differs in several respects from the consent of an individual undergoing treatment, in particular in the way that families are involved." Then there is the business of deciding what counts as being fully informed, and how exactly to go about it when people may know little of the technicalities involved.

Similarly, the principle of *confidentiality* implied by the provision of “private information” to the beryllium workers is appealing. Again, though, there are complications, as the Nuffield Council recognised. Here, they suggested that normal medical confidentiality “might justifiably be broken if an individual refused to disclose information which might avoid grave damage to other family members”.

**8**

All of this suggests that, along with the undoubted benefits which more widespread use of screening for more gene variants will bring, there will be problems, too. We cannot predict in detail what they will all be. For example, some people told they have an increased genetic risk for heart disease respond by working hard to minimise other risk factors – through exercise or healthy eating. But others hear the news fatalistically, and assume there is nothing they can do (Marteau and Lerman, 2001). More speculatively, some people appear to regard the presence of a genetic influence as reducing the possible stigma attached to a mental illness, like schizophrenia. But others seem to feel that the suggestion that there could be a gene in the family which leads to this kind of outcome is offensive in itself. It can depend on the particular culture, even the particular family.

This evidence that some genetic tests may turn out to be a distinctly mixed blessing is an argument for regarding each new testing programme as an experiment, and monitoring outcomes carefully. It also means that people may find it more helpful than in the past to learn about genes and genetic technologies, because the chances most of us will have to make sense of potentially important genetic information sometime during our life are increasing all the time (Day and Wilson, 2001).

### References

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### Further reading

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T. Marteau and R, Croyle. Psychological responses to genetic testing  
*British Medical Journal*, 316, 693-6, 28 Feb, 1998

Scope Note 22 – *Genetic Testing and Screening*. National Reference Center for Bioethics Literature.  
Accessible at <http://bioethics.georgetown.edu>

Note: all *British Medical Journal* citations can be accessed freely at [www.bmj.com](http://www.bmj.com)

**Answer the following questions on Genetic Screening**

1. This is a long article. You will find it easier to follow if you start by recognising what each section is saying. Spaces have been left for you to fill in section headings. Read the whole article and then go back and put in your headings.
2. 'Screening' differs from other tests we might have for a genetic disease, not in the test itself but in the decision on who to test. Explain this difference. (2)
3. What is the ratio of babies tested to each PKU case found? (1)
4. Even though money is spent testing every baby born in the UK for PKU the article says that the PKU test saves money. Explain how this can be true. (2)
5. Describe **three** reasons why the author says that 'You may feel that the offer of the genetic test for CF has made your life more complicated ... and more stressful'. (3)
6. Whilst PKU screening is almost universally welcomed there are far more doubts about the benefits of screening tests for a 'late-onset disorder' like Alzheimer's. Give **two** reasons why this is so. (3)
7. Identification of those whose genes make them particularly at risk and then an exclusive focus on their needs might actually have harmful effects on the overall health of the rest of the population. Describe **two** possible examples of such harmful effects from section 6 of the article. (2)
8. Having the test for a gene that increases the risk of heart disease has advantages and disadvantages. Discuss some of these advantages and disadvantages for the individual being tested, and for their family. Would you choose to have the test? Explain your reasons. (5)  
*(this answer should be a longer piece of writing, about two thirds of a page)*

quality of written communication (2)

**(20)**