We can change the future

Is genetic testing a powerful tool for determining the health prospects of our children?

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Most parents, given the chance, would do everything in their power to guarantee their children a healthy and secure future. Indeed, parents have a moral obligation to identify harms that threaten their children, and to prevent them, or at least reduce their risk, as best they can. This is so self-evident that any parents arguing to the contrary are likely to find themselves on the receiving end of public disapproval, if not facing criminal proceedings and the prospect of having the children removed from their care.

Recent advances in genetics and genomics seem to add a new tool to parents' armoury of measures to protect their children's health and well-being. The clear causal link between genes and disease was demonstrated convincingly by the antenatal detection of a particular mutation which ultimately leads to the emergence of Huntington's disease 45–50 years later. The predictive power of genetics offers the prospect of identifying our future health status, so as to intervene in ways that will prevent diseases emerging, or will catch them early enough to nip them in the bud.

But is this really the case? Or is it likely that the hope we have for our children will be manipulated by the hype of those with vested interests in promoting the use of genetics in areas where its application is inappropriate? Perhaps the science has not yet caught up with our ability to imagine creative applications for this new technology? Perhaps there are downsides to knowing our children's genetic information, which could outweigh any positive benefits that may accrue? These questions have aroused enormous interest not only among parents but also within healthcare systems worldwide. At first glance, genetic testing may sound like a good idea: if we can identify health

Illustration: Simon Walter

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risks early on, proper treatment or preventive action may both benefit the child and relieve national healthcare systems. However, as I will argue, we are nowhere near a scenario in which genetic testing for a

wide range of diseases, whether mandated or instigated by concerned parents, will have much of an impact.

In a recent White Paper, the British Government raised the possibility of introducing wide-ranging genetic screening programmes for all babies born in the UK (Department of Health, 2003). Among other things, it suggests "... to screen babies at birth... and to produce a comprehensive map of their key genetic markers, or even their entire genome." The rationale was that "... the baby's genetic information could be securely

stored on their electronic patient record for future use. It could then be used throughout their lifetime to tailor prevention and treatment regimes to their needs as further knowledge becomes available about how our genes affect our risk of disease and our response to medicines." Clearly, at the time the White Paper was written, someone at a senior level in the UK healthcare system held the view that genetics could be highly predictive of future health.

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Similarly, officials in the USA also seem to adhere to the view that genetic testing of children will safeguard their future health. In February this year, *The New York Times* reported that a federal advisory group was about to recommend that all newborns should be screened for 29 rare diseases (Kolata, 2005). While various governments still ponder whether they should introduce screening programmes for all newborns, the private sector has already moved ahead to meet the increasing demand among parents and health-conscious adults. Private companies, such as Quest Diagnostics (Lyndhurst, NJ, USA), already offer a wide range of tests for sale, usually, but not necessarily, mediated by a physician, to diagnose or predict a patient's medical condition. Many of these are genetic tests that analyse a patient's DNA or chromosomes, or they may be physical or biochemical tests, but they all reveal information that can be interpreted in relation to the patient's genome.

Is this a bad thing? After all, if you want information about your child's health and the risks he or she might face in the future, shouldn't you be allowed to have it? Who has the right to stand between you and your wish to know? To be fair to the company mentioned above, their website (www.questdiagnostics.com) is littered with good advice to those contemplating testing. It stresses the need for genetic counselling and draws attention to the implications of being tested. Not all organizations may be so scrupulous in their

business practices, and not all physicians are equally competent in explaining what genetic tests may or may not reveal about a particular disease or disorder and its genetic components. Does this matter? Genetics is, after all, the key to the future, and a powerful tool to enable us to control our children's destiny. Unfortunately, real life is far more complicated than we might hope, and the promise demonstrated by the power of a genetic test for Huntington's disease is rarely replicated elsewhere.

Any discussion of technological progress is almost outdated as soon as it is written. To address some of the clinical, social, ethical and familial issues associated with genetic tests for children, I therefore make the assumption that it is possible to provide an accurate analysis of all—or at best, of any interesting parts—of an individual's genome quickly and cheaply. I know this is not the case, but enthusiasts claim that it soon will be and even pessimists tend to agree with them, although estimates for achieving this goal range from just around the corner to 50 years hence.

Notwithstanding the availability of such tests, parents seeking knowledge about their child will turn to their doctors—and increasingly to other sources of information—for advice and support. Clinicians should therefore ask themselves a number of questions before suggesting a genetic test for a child. Why is it a good idea to test the child and what will the test reveal that I do not know already? Will I understand the results of the test and will I be able to explain them to the parents? Is the information sufficiently significant to make a decision and what else could a test reveal? What will it enable me to do, which would otherwise not be possible?

Parents might be well advised to consider the same questions before having their children tested for possible future diseases. However, decisions are rarely made in a calm, rational way and after mature consideration of all the relevant information. In the real world, both patients and professionals are under pressure. They have limited understanding, they are influenced by marketing, their motivations may be mixed and their expectations are unrealistic. Nevertheless, decisions are made, tests are offered and carried out, and the results are acted upon—more often than not for the better, or so it would seem.

The difficulties in performing genetic tests and analysing their results have meant that tests have generally been used in special cases—when children have a significant risk of developing a severe disease or to confirm a previous diagnosis—and in a clinical context with access to counselling and other support services. Physicians usually offer these tests to enable parents to make informed decisions about the prevention and treatment of particular diseases, or about reproductive choices, to avoid having children with the condition. As the diseases tested in these settings are usually severe, a mindset has developed which regards all disease genes as highly penetrant (expressing themselves largely independently of environmental factors), usually of adverse impact and surprisingly common. Furthermore, the lesson often drawn from rare but highly penetrant genes is that they are inexorable in their impact.

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Although this may be true for some diseases, and Huntington's is usually used as an example, it is far from the case for most. Even in highly penetrant single-gene disorders, there are often interventions available to mitigate the worst effects, for instance in the treatment of phenylketonuria or familial hypercholesterolaemia. Nor is it the case that the discovery of familial diseases comes as a complete surprise. Most families have a sense of the diseases that affect them more than others, even if their assumptions are not drawn from an understanding of biology that is recognizable to a molecular geneticist.

As genetic tests are increasingly offered to diagnose the future risk of common complex disorders, patients, parents and even physicians run the risk of transferring uncritical assumptions, experiences and conclusions based on highly penetrant single-gene diseases to complex diseases. However, complex disorders are, by definition, complicated. They arise from the interaction of a large number of factors, some of which are genetic, some environmental and some related to lifestyle. Our

understanding of these factors and how they interact is generally very limited. It took many years and epidemiological studies involving tens of thousands of people to demonstrate conclusively the link between tobacco smoke and lung cancer. Still, some people claim a causal link between a few genetic factors—sometimes from small, unrepeatable studies—and the emergence of a common complex disease. Focusing on these assumed causal links not only is bad science, but also may neglect other, more powerfully predictive factors. It may not even make a difference with regard to advice or interventions, as things known to reduce the risk of future disease in those particularly at risk are often good for the rest of us too. Rushing to test a child for a range of adult diseases may therefore not necessarily add anything to one's knowledge of how to improve their future health.

Of course, where there is a strong enough link to allow predictions to be confidently made, and where there is action that can be taken or avoided so as to prevent the disease, then this is a different matter entirely. In such cases, the arguments against testing are much weaker, given the moral imperative to avoid harm to our children's health and well-being. In many countries, the state actually intervenes to ensure treatment of children when parents seek to prevent it for some reason.

The genetic testing of children is not just a medical matter. It can create implications for other family members and for the child's future status, both within the family and with regard to society as a whole. With rare, highly penetrant genes, there is a risk that other family members will be affected—but this risk existed before the decision to instigate a test. What to do about it, and how the communication within the family is handled, is potentially fraught, but so is the birth of a severely sick child resulting from a failure to reduce the chance of an avoidable harm. In diseases with low-penetrant genes, however, this risk is often more imagined than real, and creates an additional responsibility for those advocating the use of tests. They have to ensure that their explanations are clearly understood when the test results are divulged to parents.

Similarly, in a broader, social context, there is a risk of building on shallow scientific foundations. Such an exaggeration

of the predictive power of genetics also creates fears of stigmatization for those who receive a negative diagnosis. Furthermore, it could lead to the medicalization of children who are currently healthy and for whom the prospect of developing a given disease is by no means certain. For them, the loss of the opportunity to be seen as healthy may be more damaging than dealing with the predicted disease if and when it arises.

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Fear of negative consequences, for example, difficulties in employment, or of securing insurance, is often cited as another reason to avoid predictive testing. This fear is real, even if it is based on a false perception of the actual legal and scientific situation. This may become a disincentive to predictive testing, even if tests can produce information that is beneficial to the well-being of a child by allowing targeted interventions to catch a disease in the early stages when it can be treated more easily. In such situations, there is almost a knee-jerk reaction to prevent misuse of testing through regulation or legislation. A better approach might be to implement educational campaigns that explain the potential for genetic testing, and to decide on its relevance in the light of other significant factors. Ultimately, it is likely that those who might see genetic test information as a shortcut to decisions will come to realize that it is in fact nowhere near as powerful as they might have hoped.

Faced with increasing technological possibilities and rising consumer demand, healthcare professionals can find themselves between a rock and a hard place when it comes to testing children. Providing patients and families with healthcare whilst distinguishing between wants and needs, and making effective and efficient use of public money, is a potentially thankless task. When a genetic test can yield significant and reliable information that will have an impact on the future health of a child or the reproductive

decisions of parents, there seems to be an unquestionable case for such tests to be offered. If not now, then in the future, the number of such tests may increase and the costs will decrease substantially as commercial systems improve and expand on present 'home brew' practices. This will improve the quality and in many cases the quantity of life for children and families throughout the developed world and, increasingly, in the developing world too.

However, just because something can be done, and families want it to be done, does not create a requirement that public funds should be used to make it happen. Where the science is lacking, and where the value of a genetic test on a child is limited, the obligation on the public healthcare system is redundant and tests should not be offered. Similarly, if a test does not provide an advantage for the child or does not relate to parental reproductive decisions, it is arguable that the compromise to the child's autonomy—in the removal of their right not to know about future health risks—may outweigh the possible benefits. There is scope for a sound dose of common sense here. Whereas the diagnosis of a mutation that will cause Huntington's disease later in life seriously compromises a child's future, the discovery that he or she may face a slightly elevated risk of cardiovascular disease is unlikely to be seriously prejudicial to a child's mental and physical well-being.

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Of course, all this may change. With greater knowledge, we may be able to make highly accurate predictions on the basis of sophisticated analyses of children's genomes, and factor in the many lifestyle, dietary, socio-economic and environmental components that play their part in the development of common complex diseases. Personally I doubt it, at least for the foreseeable future, but if it does occur, then such a development will not happen overnight and we will have time to adapt our thinking accordingly.

In the meantime, should we stop parents buying genetic tests for their children over the counter if the healthcare system does not pay for them? Probably not—provided the requirements of consumer protection and trading standards legislation are vigorously enforced, the goods are fit for their purpose and the information from the purveyors is robust, clear, comprehensive and comprehensible. I have faith in the common sense of parents and although there may be an initial enthusiasm for purchasing genetic tests, I believe this will quickly pass. People will come to realize that the results are of little practical value in the real world, that the advice that testing

precipitates is probably bland to the point of banality, and that there are better things on which to spend their money. But if it is acceptable to take your child to an alternative therapist whose practice may have no scientific underpinning, it should also be acceptable to use services that at least have some grounding in molecular biology and that are potentially amenable to investigation and criticism.

If that is what parents want to spend their money on, why should we try to stop them? After all, their desire usually arises from a motivation to do the best for their children. That must be praiseworthy even if we feel that the chosen route is misguided.

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