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Genetic testing services in Europe: Quality assurance and policy issues

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Abstract The popular press is painting a picture of a future in which everyone has a detailed DNA profile of themselves drawn up. Such a vision of the future, however, is more science fiction than science practice. Predictive tests for complex diseases and cancer, eg colon cancer and breast cancer, are increasingly being used, and the related, and important, genetic counselling may become complex and comprehensive.

Quality assurance in genetic testing for both cytogenetics and molecular genetic testing in Europe is also described. The quality of genetic testing in Europe could be substantially improved, and before a genetic test is accepted as a routine diagnostic or prognostic procedure it should have proven clinical utility. Pharmacogenetic testing looks at the efficacy of medicines and their side effects on patients and patient groups, and is increasingly being used to develop better targeted medicines.

Genetic testing services and genetic counselling are structured in different ways in Europe, and organisation and reimbursement differ among European countries. Quality and non-directive genetic counselling must be made an integral part of quality genetic testing services, and be sufficiently reimbursed. European networking and identification of reference centres for quality-based diagnostic testing of genetic diseases should be encouraged. Reimbursement within Europe for sample forwarding should be adapted to allow samples to be tested in countries other than the country of origin of the patient.

Keywords: genetic testing, quality assurance, counselling, pharmacogenetics, patients, society

Introduction

The popular press is painting a picture of a future in which everyone has a detailed DNA profile of themselves drawn up, useful for disease prediction and treatment selection now and throughout their lives. Quite apart from the scientific improbability of this scenario (it is extremely unlikely that genetic information no matter how carefully

it is mapped and understood will allow such a deterministic vision of our future to materialise), the complexity of the technology and the sophistication of healthcare systems that would need to handle the sheer volume of information generated for each of the 350 million citizens of the European Union, put such a vision of the future firmly into the realm of science fiction, not science practice.

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On the other hand, genetic testing has been used since the 1960s for both prenatal and postnatal applications. Genetic tests can be performed on clinical samples originating from a foetus (prenatal testing), on early embryos (pre-implantation testing) or on children and adults (postnatal testing). Cytogenetic testing, ie chromosome analysis on dividing cells from amniotic fluid or other clinical samples, visualises chromosome abnormalities such as trisomies – three chromosomes of the same type instead of two – translocations or deletions. Cytogenetics is also being used in the diagnosis or confirmation of cancer and can be complemented by newer molecular cytogenetic techniques, including FISH (fluorescent *in situ* hybridisation) or CGH (comparative genome hybridisation) for more subtle changes in the chromosome structure or for studies on non-dividing cells.

Since the 1990s, molecular genetic testing, looking for deleterious changes in human genes, has increasingly been used to detect gene defects. Such molecular testing studies changes in the composition or structure of DNA, RNA or even proteins using molecular techniques, such as polymerase chain reaction (PCR), quantitative PCR, mass spectrometry or sequencing. These methods are all different ways of detecting changes in the composition of genetic material. Single gene disorders, caused by defects in a single gene resulting in the absence of a critical protein or the presence of an abnormal protein, are being searched for and diagnosed with the help of such techniques. Cystic fibrosis, for example, is a rather rare condition, but presents itself through more than 900 mutations, most of them very rare, with a frequency of much less than 0.1 per cent of all diagnosed cases in the population. Many other so-called multifactorial disorders also have a genetic component, which may involve several genes interacting with an individual's lifestyle or living environment.

Some of the methods used in genetic testing have been or are being automated, but many must still be performed manually. Indeed, automation is only gradually

becoming available and only a limited number of diagnostic kits are commercially available, mainly for well-characterised diseases with well-studied mutations which have been identified years ago. In addition, many different DNA defects can be responsible for the same or similar clinical symptoms, and these defects may even have different regional frequencies in Europe. This further complicates standardisation of procedures or kits. Diagnostic methods for genetic testing are no longer used exclusively in genetic laboratories. The identification of changes in DNA, RNA and proteins relevant for the diagnosis and therapy of somatic diseases, such as cancer and infections, has created a large number of additional applications of these methodologies in practically all medical specialties. As a result, they have also become basic tools for most clinical chemistry and clinical biology laboratories.

Another area that is growing rapidly is pharmacogenetic testing. This technology tests the efficacy of medicines and their side effects on patients and patient groups, and is increasingly being used to develop better targeted medicines. The potential consequences of pharmacogenetics on the development of medicines from a research, clinical trial, regulatory process and marketing point of view are staggering.

Clinical use, counselling, regulation for genetic testing and accessibility

Before a genetic test is accepted as a routine diagnostic or prognostic procedure it should have clear clinical utility, meaning that the test should help the medical staff in diagnosing and treating or counselling a patient. Providing diagnostic or predictive genetic testing is not just the provision of a test result to a doctor or a patient, but should also include, depending on the disease being looked at, the provision of non-directive and professional genetic counselling to the patient and sometimes family members. For genetic testing, the decision to test and the evaluation of its

results should always occur in the context of a genetic counselling session.

Predictive tests for complex diseases and cancer, eg colon cancer, breast cancer, are increasingly being used, and the related counselling may become complex and comprehensive. The correct meaning and consequence of the test will have to be explained in detail to the individual if they are to understand its precise meaning or limitations. The knowledge of genetics in the general population and even in the medical profession is still very limited. Over the counter testing or testing on the request of a physician who does not grasp the full significance of a test result could have serious consequences for a patient.

Therefore, counselling is an extremely important part of the process of explaining a test result to a patient, determining the way they may cope with a test result, and should be valued as such in the healthcare system of tomorrow. Since these counselling sessions are essential but also expensive, in view of the time spent with the counsellee, it is becoming very important to provide sufficient and appropriately trained counsellors and financial support.

Genetic services and molecular genetic testing laboratories in particular are structured in different ways in Europe. In some European countries, eg in Benelux, the services, including genetic counselling, are restricted to genetic centres that offer 'total' care to the patients and their families. Access to these facilities is either through the family physician or directly via the geneticist. In other European countries, such as Germany, only specific aspects of the services are regulated, eg genetic counselling or some aspects of prenatal diagnosis, while all other services are provided by whomever wants to provide it. Finally, many European countries have no regulations and as a consequence, 'self-made' geneticists, with or without experience or training, with or without quality control, provide services. The majority of the European countries do also not recognise the specialty of human genetics as a separate medical specialty, so the European Society for Human Genetics

(ESHG) is currently calling for this recognition.

Organisation and reimbursement of genetic testing

Samples to be analysed can be referred to a testing laboratory, when available. Depending on the expertise and the equipment of the laboratory, some laboratories will test for all possible variations and mutations a particular gene while others will only test for a limited set of mutations. For many rare diseases, however, the prevalence is so low that no expertise can be found in the immediate geographical vicinity, or the equipment and expertise may not allow a local laboratory to provide a full investigation. In that case, the clinical sample must be forwarded to another laboratory. In view of the many inherited and somatic diseases that are being identified (more than 1,000 at present and 11,000 more to come¹), based on intensive research efforts and on the recent publication of the Human Genome Sequence, it has become almost impossible for any single laboratory to provide testing for all identified diseases. Samples are therefore being sent to specialised laboratories in Europe or in the USA. For diagnostic samples, such networking is very difficult, because of the different legislation and related reimbursement in each European country. Some countries, such as France and the Netherlands, forbid diagnostic testing of patient samples outside their borders, or do not reimburse such testing services.

The lack of reimbursement for genetic testing, when done in a country other than the country of residence or social security subscription of the patient, based on geography, hampers equal availability of good genetic testing services to all citizens even within the EU. In some European countries, such as the UK and the Netherlands, genetic testing when done within the national healthcare system is fully reimbursed as part of the overall

health services to the regional population. In other countries each type of test is reimbursed at a specific rate by the national health insurance system. This may or may not include a restriction to have the testing done in a genetic laboratory and to have the patient pay a rather symbolic personal contribution. Also of increasing importance are efforts to determine reasonable reimbursement rates for adequate genetic counselling, because in Europe, counselling is not always part of what is reimbursed while it is an extremely important part of the package.

Some private insurance systems will cover public or private testing while others will not, and some will cover testing in a foreign country while others will not. It is clear that there are about as many systems as countries in Europe and that depending on where one lives a service can be available, partially or fully covered or not at all. In other countries, outside the EU, the USA and Japan, major problems may either be the cost of the testing, incomplete or total lack of reimbursement, or the availability of a counselling centre located sufficiently close to the families in need.

Quality assurance in genetic testing

Cytogenetics

Cytogenetic testing, although existing since the 1960s, demonstrates no uniform quality in Europe. The number of cells being looked at per sample, the banding quality and the turn-around time are not standardised, and no minimum European quality norms are set. In addition, many small laboratories performing cytogenetic testing all over Europe only see a few abnormal cases per year, which raises concerns about the experience level of the personnel performing the testing. Quality improvement is possible at the laboratory level, by quality testing of reagents, by installing standard laboratory operating procedures and appropriate quality assurance protocols. Additionally, the clinical genetic training of physicians

assures consistent evaluation of genetic test information before it is provided to the patient.

The quality control programme installed in the UK is probably the best known in Europe. In this paper, Germany is used as an example of a country where quality assurance and quality control (QA/QC) measures in genetic testing services are required by law and implemented by the scientific societies or professional organisations. A formal qualification (specialisation in human genetics) is required for medical doctors as well as for PhDs in the provision of genetic testing services in Germany. This is a direct consequence of the inclusion in German social legislation (book 5) of QA/QC as a permanent commitment to genetic testing service providers. According to recommendations of the Federal Medical Council, an external quality assessment scheme for cytogenetics was established as a pilot project in the late 1980s and introduced nationwide in 1993. The quality of the chromosome preparation is assessed by a commission using a scoring system developed by the British Association of Clinical Cytogeneticists.² In addition, the turn-around time (TAT) for cytogenetic analysis of a sample is recorded. At present there are more than 80 participating laboratories.

In accordance with activities to harmonise standards and guidelines within Europe³ an exchange of ideas and/or collaborations with several countries including Switzerland and Austria is beginning. Observations based on the past ten years following the introduction of the German QA/QC scheme for service cytogenetics include increased quality of pre- and postnatal chromosome preparations and no apparent difference in quality between academic and private laboratories, while turn-around time for private laboratories is somewhat shorter.

Molecular genetic testing

The limited number of studies performed to date have clearly shown that the quality of

molecular genetic testing in Europe could be substantially improved. The lack of stable positions and training of academic personnel due to vagaries of funding, and the lack of standard laboratory operating procedures in academic settings contribute to the issue. Two initiatives have been funded by the European Union to organise quality assessments. The European Molecular Quality Network (EMQN), a project funded by the EU to set up pilot studies for external quality assessments of laboratories involved in genetic testing as well as to draft best practice guidelines for these tests, has shown in its three year existence that molecular testing for Huntington disease, fragile X, breast cancer and a series of other diseases is subject to unacceptable error rates with dramatic consequences for the tested individual, and can be improved with appropriate quality assurance programs. As a further example, the Cystic Fibrosis Thematic Network, financed by the Framework V programme of Directorate General Research of the European Commission, has organised external quality assessments for close to 200 laboratories in Europe over the past five years. Initially, more than 30 per cent of the laboratories made technical errors in the assessments. Through training and information, this error rate has dropped in the past two years to approximately 6 per cent.

Within Germany, national quality assessment schemes for molecular genetic testing were introduced in 1994. At present there are 11 disease-specific programmes chaired by individuals with proven expertise acting in collaboration with a commission of the Professional Organisation for Medical Genetics covering the most important laboratory methods. DNA samples are sent to the participating laboratories and testing as well as reporting performance is assessed using a numerical scoring system. The experience of the past five years shows a number of common factors. These common factors include at least one misdiagnosis in all schemes, with the exception of myotonic dystrophy, and, unexpectedly, an error rate, different by

disease type and by year, not correlating with the technical difficulty of a particular test. For cystic fibrosis for example, in the year 2000 there were eight diagnosis errors and one report error in 288 cases. In general, for all diseases, some of the errors appeared to result from inadequate internal quality management, while other errors originated from the application of non-validated methods or inadequate reporting. Errors were not found to cluster in a small number of 'incompetent labs' but also affect facilities considered experienced. There is a tendency towards improvement in quality of molecular genetic testing, although this is not easy to quantify. The development of guidelines in addition to those already in existence and good laboratory practices (GLP) workshops were helpful in improving the quality of genetic testing. Horsthemke⁴ raised concerns about the performance of the participating German laboratories specifically with respect to methylation assays and microsatellite analysis, reporting an overall error rate of approximately 8 per cent since 1998.

To our knowledge, comparable figures do not exist for other regions. From these European assessments it has become clear that there is also an international need for testing standards. Indeed the absence of standards prevents unequivocal validation of commercial or home-brew diagnostic tests. For this reason, the EU has decided to fund a four-year project to develop such standards (the CRMGEN project), planned to start late in 2001. In addition, further training and systematic external quality assessments will be required to bring genetic testing services up to an acceptable level. It will undoubtedly be necessary to install some form of laboratory accreditation at the national and preferably at the European or even international level. This was also recognised during a workshop organised by the Organisation for Economic Collaboration and Development (OECD) in Vienna, Austria in February 2000.⁵

Accreditation, if designed specifically for genetic testing laboratories, will clearly identify laboratories that can provide a reliable diagnosis, and an acceptable and

reasonable turn-around time. Staff competency testing, incident tracking systems, performance measures, quality control monitoring and a follow-up programme comparing laboratory results to patient outcomes will help assure accurate testing. Accreditation and accurate testing may also help to solve the matter of reimbursement and networking between accredited laboratories, since the different countries would not be able to invoke quality as a reason not to allow testing in another country. Moreover, regional reference centres with proven expertise for the identification of particular genetic defects could be identified in such a system.

Pharmacogenetics: potential and consequences

Mechanisms of disease, individual genetic variation, therapeutic response and genetic predisposition will all be the beneficiaries of the knowledge developed as the result of the Human Genome Project (HGP). The use to which this information is ultimately put will decide the true value of this huge project. The impact of this information flow on drug development will significantly change how new drugs are registered and how existing therapies are used. It is unlikely, at least in the foreseeable future, that one's entire genetic makeup will be recorded for clinical use. As discussed earlier, the use of genetic information to provide better care has been in regular practice for decades. The fact that individuals respond differently to drugs, even to the extent that people may die as a consequence of drug side effects, has been part of common medical practice for over half a century. Using the new information, the pharmaceutical industry routinely tests clinical trial populations for variants in drug metabolism genes that augur severe adverse reactions. The increase in information provided by the genomic revolution is resulting in a greater number of genetic tests valuable in predicting individual response to therapy. The quality of such testing will

affect the ultimate utility of the information being derived.

The introduction of testing intimately tied to therapeutic administration is already a reality with testing for *Her2* determining Herceptin™ administration in the treatment of breast cancer, and *bcr/abl* analysis playing an important role in the selection of Gleevec™ therapy for chronic myelogenous leukaemia. The number of these types of tests will inevitably increase over time, while the range of test types will include immunohistochemistry, single nucleotide polymorphism analysis, standard cytogenetic analysis and *in situ* hybridisation. The identification and announcement of markers linked to therapeutic selection, diagnosis, prognosis or predisposition will outstrip the current ability of the medical community to critically evaluate the clinical utility of each marker. Without appropriate quality assurance methods, test validation procedures and guidelines, the genetic assays of real value will be mixed with those that have little or no value. Such an outcome will be contrary to the goals society put forward for the Human Genome Project.

The role that broad population-based genetic testing for the purpose of providing a DNA profile will play in the future is unclear. The position taken by genetic testing laboratories concerning the provision of genetic information has traditionally been to test only for specific conditions or markers as requested by a qualified medical professional. This limits the inadvertent discovery of genetic information that may impact an individual in ways not anticipated when the decision to have testing performed was made. Current medical practice is unlikely to support the provision of unsolicited information when there is no available treatment or prevention plan beyond counselling lifestyle changes. In addition to the difficulties inherent in performing testing without a specific outcome, the current level of technology does not support this type of testing. If one postulates a hypothetical US\$200m drug and links a genetic test to the administration of that drug, the number of tests required

for new prescriptions per year could be in the range of 200,000. This would be nearly double, for example, the current number of cystic fibrosis tests performed annually in the USA prior to population screening. If this pattern were repeated for a number of drugs, the ability of the genetic testing community to perform such testing would be rapidly exceeded. The incorporation of this type of genetic testing into routine clinical practice will require the development of novel technologies having the accuracy and reliability assumed as a standard for other routine clinical laboratory tests. The propagation of such testing will require clinical trials to validate the accuracy and reliability of the markers as well as the laboratory procedures that are involved.

Appropriate quality assurance methods will also be necessary for the effective development of pharmacogenetic testing procedures in the future, thereby again pointing to the needs identified for diagnostic genetic testing. The identification of a marker thought to be clinically relevant is but the first step in a process. Establishment of relevant clinical data demonstrating the value of the marker and peer-reviewed publication of that information is essential prior to the acceptance of the marker. The evaluation of the marker by a peer-reviewed publication method is a valuable part of the process in the widespread adoption of a clinical genetic test. This process avoids endless repetition of clinical trials by each provider and allows the widest possible review of the data. Once the value of a marker has been established, each laboratory considering provision of such a testing must consider the design and implementation of the assay in the context of appropriate quality and design control. The development of standard procedures within each laboratory for assay selection and design control will be essential as the number of tests being introduced increases.

While the level of genetics expertise in the medical community needs to improve dramatically, genetic testing is beyond any doubt an area of significant future growth.

The pressure on the medical community to incorporate genetic information in their selection of treatment options will come from scientific advances, the pharmaceutical industry, regulatory agencies and the public. The incorporation of genetic tests and genetic information in clinical trials and treatment provision will have a significant and long-lasting impact on the practice of medicine.

Benefits and risks, industry involvement and societal issues

Genetic tests are undoubtedly of major value in the medical diagnosis of genetic disorders, especially since many disorders seem to have a genetic component. Prenatal testing provides valuable information to assist women in making an informed decision about their pregnancy. The provision of rapid, accurate information is of crucial importance for these women, making turn-around time one of the performance indicators for prenatal testing. Postnatal diagnosis provides confirmation of diagnosis, or may be used in a predictive way. The provision of predictive genetic testing when insufficient clinical data are available for a test, or for a disease for which no cure yet exists, may raise ethical issues. Another ethical issue may be related to the issue of informed consent: indeed a patient should be fully informed about the test and its consequences before consenting to it, and has the right to refuse to undergo testing. In addition, society should use genetic test results confidentially and at the least with the same care as other medical information. This means that one has to avoid negative discrimination based on genetic test data, eg for insurance or employment.

In some European countries, such as Germany, Switzerland, Italy and Spain, genetic testing is increasingly being performed by private organisations. Responsible private providers are also concerned about the issues of privacy, confidentiality and negative discrimination, and have been participating, and will continue to participate, in the dialogue to

create policy for these issues. In recognising the sensitivity of the area, responsible industry players involved in genetic testing as a whole have been fairly cautious in introducing new genetic tests. In addition, informed consent and education of patients and physicians have been and will continue to be taken seriously by them. Responsible industry also understands the need for high-quality counselling services as part of the total service package.⁶

One unusual feature of the genetic testing services is that the few industry players find themselves competing with non-profit organisations. Still, industry believes that, because of its organisational expertise and standard operating methods, it is well placed to provide high-quality genetic testing services, which are rigorously quality controlled. In order to do so, partnerships with academia, with patient groups and with healthcare systems may emerge in the future.

It is clear that genetic testing and related issues may have an impact on the fundamental rights of any individual. Full access to genetic tests when these are of the utmost importance to obtain a correct diagnosis, to determine the risk to develop a particular disease, to determine a carrier status or to be able to start an appropriate treatment, should indeed be considered as a basic right. Poor quality of test results will have dramatic consequences for individuals, who are erroneously identified or not identified as carriers of gene defects that are life-threatening, or who make the decision to stop a pregnancy. Inaccessibility of the service because of financial reasons is discriminatory, while refusal to send a sample to a foreign laboratory for regulatory or financial reasons is irresponsible. These issues will become gradually more important as the number of inherited diseases that can be tested increases. Also, the rapidly increasing applications of the same methodology in sporadic or acquired somatic diseases, such as cancer, leukaemia and infectious diseases, will necessitate a better organised laboratory service than in the past. Moreover, the not-too-distant future will bring testing for the genetic

predisposition to frequent societal diseases, such as diabetes, osteoporosis, asthma, rheumatic disease, psychiatric diseases, Alzheimer's and Parkinson's, among others. Clearly, the available facilities for genetic testing will soon drown under the requests. If at that time no European consensus has been reached about how all this testing will be done and how it will be financed, the rights of patients are at serious risk and negative discrimination will flourish. The European Parliament has created a Temporary Committee on Human Genetics and other New Technologies in Modern Medicine, to look at these issues, and is organising hearings with experts and with the civil society to discuss them.⁷

Indeed, following the decision in the UK to extend the Human Fertilisation and Embryology Act (1990) to allow the use of human embryos in tightly defined research, the European Parliament passed a resolution that sought to deny access to EU funding to those institutions where work on human embryos was undertaken. In the debate around this proposal a decision was taken to set up a special committee of Parliament members to examine the ethical and social consequences of development in human genetics and modern medicine, which were perceived to be potentially problematic. This committee is due to report to the plenary session of the Parliament in November 2001.

Like all European Parliament committees the temporary committee on genetics includes members from across the political spectrum. Its terms of reference give it almost complete freedom of action to pick and choose the issues that it deems to be of significance and that it chooses to address. In order to produce a draft resolution, members of the committee held a series of open meetings at which they heard evidence from a range of interested parties, representatives of whom were invited to make written and oral presentations to the committee. Among those invited were academic scientists, doctors, representatives of the biotechnology and pharmaceutical industries and delegates from patient support groups, disability organisations,

religious bodies, women's groups and others. Those selected were inevitably determined by reference either to contacts known to the committee members and or its secretariat or those sufficiently 'on the ball' to make their presence and their wish to contribute known. Given the task facing the committee, the time-scale allowed it by the European Parliament and the resources available for it to undertake its task, it may be easy for critics of its work to pick holes in both the process and the outcome (which at the time of writing is still to be determined). However, it is clear that the robust approach of the chair, Robert Goebbels will go a long way towards preventing the Committee's procedures being hijacked by vested interests either uncritically in favour of science or unreasonably opposed to the new knowledge arising from genetic research and its application for the resolution of complex medical, social and ethical issues.

Among the difficulties facing the members of the Committee is the need to beware of seeking unity when diversity is more legitimate, particularly with regard to ethical questions. There is no general European ethic on genetics and attempts to develop one are likely to result in statements that are either so bland as to be worthless or so rigid as to be unacceptable. The members of the committee will, it is to be hoped, recognise that there has been a due process undertaken in some of the member states and that decisions taken have a validity in that member state.

The report of the Committee's deliberation and the resolutions that it passes will eventually form a background to considerations by the Parliament and the Commission for decisions to be taken in respect of, for example, the Sixth Framework Programme. In a fast-changing field such as genetics it must be recognised that any report and recommendations will have a limited shelf-life and that new knowledge may alter perceptions significantly. Hopefully the wisdom of the members of the committee and of the European Parliament as a whole will ensure that no matter how helpful or otherwise the committee's resolution in the short term,

they will not be the last word on this important subject.

The patients

Try to put yourself in the position of someone receiving genetic information. People do not decide to go to get tested on the spur of the moment. It is not a 'What shall we do today – go shopping or get my DNA analysed?' type of decision. Rather the need to know what might be in your genes arises because some external event creates anxiety about your current or future health or that of your (unborn) child.

It may be that someone knows of a disease such as cystic fibrosis in her family and wishes to find out if the baby she is going to have will be affected. It may be that her mother and her mother's sister both died of breast cancer in their 40s or it may be for some other serious reason that a person finds himself in the situation where the need to know exerts itself. Whatever the precipitating event it is likely that the circumstances that create the need to seek genetic testing will be seen by the patient with a certain degree of stress and a high degree of concern. This being the case people are likely to approach the acquisition of genetic information with feelings of anxiety – possibly even fear about what they may be going to find out – uppermost. Coupled with the fact that most people have little understanding of genetics and where the limits on genetic prediction may realistically be drawn and a situation is created where stress and uncertainty predominate. So what do people expect of the test procedure? What helps them to make the best of the situation in which they find themselves and empowers rather than disables them? They need to be able to make informed choices, rather than being pushed along by chance – even if this means choosing the least worst outcome, rather than a good one. In such a situation patients need reliability of test results and honesty: clear and unambiguous information. They want an accurate test and precise communication of information in a way that

is appropriate and usable, not clouded by too much jargon.

The language of DNA is commonplace in society, yet investigation often reveals that this apparent genetic literacy conceals a deep well of confusion and misunderstanding about genetics. The apparent precision of DNA-derived results, rightly or wrongly – often fuelled by media images of the accuracy of forensic uses of DNA evidence in serious crimes – may mean that many place a higher value on the predictive value of the result than is warranted. After all, if DNA analysis can tell that there is only a one in a million chance that a person whose DNA matches that at a crime scene is not guilty, then surely it can tell me whether I'm going to get breast cancer or not? Communicating uncertainty is difficult and there is no absolutely guaranteed method that will work every time. As a consequence a variety of different strategies must be employed to ensure mutual comprehension.

Yet it is important to be clear in the message given or people will not be able to use this new knowledge and make decisions. It is also important to be clear about what test results do not tell you. Knowing what inferences you cannot draw can be as useful as knowing those you can. Giving reasons that explain why things are as they are can also help patients to contextualise and to accept or reject the service being offered. As a general rule it is easier to accept reasons for an inability to be precise that are 'real' – such as the fact that research has not yet discovered a gene that causes XYZ condition or the biology does not work that way so we cannot tell you – rather than those that are 'systems driven'. For patients waiting for a result, the need to collect a batch of samples to make analysis 'economic' or the fact that a test used to be available as part of the research programme, but now the project has concluded, is deeply frustrating.

By and large patients do not have strong views about where and how genetic tests are done. Organising the service and using the best available technologies are usually thought to be the responsibilities of

professionals. What patients do care about is the context in which the outcome of testing is to be delivered and the access to information advice and support (from a diverse range of sources if they wish to access them) that is facilitated for them. If this goes well then information, even if it is fundamentally bad news – 'I'm very sorry Mrs Smith, but the test results are positive and you do have the mutation' – can be dealt with and assimilated in such a manner that people can make good decisions that they feel to be right for them. A quality genetic testing service will be set up in such a way as to ensure that this happens to the fullest possible extent.

Conclusions

With the progress of the Human Genome Project, more and more pre- and postnatal genetic tests are being developed with diagnostic or predictive impact. These tests are likely to play an increasing role in the provision of healthcare and related services. Genetic testing therefore comes under the spotlight of society through press coverage on the patenting of genes, the relationship between genetic test results and life insurance or employment, and by the relationship with the development of medicines of the future. The main question is and will be how to use these new developments to the benefit of patients, without negative discrimination or stigmatisation, and by providing sufficient and honest information for the patient to understand what they have learned. Medical doctors and patients choosing to take advantage of these genetic tests will be able to make more informed decisions about health and lifestyle.

It is up to our society and its leaders to make sure that the benefits offered by technological progress in this field are used in a positive way and that the quality of the genetic tests offered is high. To fail to do so would open genetic testing to an environment fuelled by unjustified fears and misinformation, thus depriving the public of medical knowledge increasingly valuable to their health. Therefore, quality assurance of

genetic testing, and accreditation of genetic testing laboratories should be organised on a European or even international level before the confidence of society in genetic testing is badly undermined.

Efforts should be increased to ensure that quality and non-directive genetic counselling is made an integral part of quality genetic testing services, and is reimbursed as part of the package. European networking and identification of reference centres for quality-based diagnostic testing of genetic diseases should be encouraged. Reimbursement within Europe for sample forwarding should be adapted to allow samples to be tested in countries other than the country of origin of the patient. Finally, participation in national, European (EMQN) or other quality assurance programmes should be encouraged for all laboratories involved in providing any kind of medical genetic testing services.

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