APPLICATION OF MOLECULAR GENETICS IN CLINICAL PRACTICE

Completion of the sequence determination of the human genome in April 2003 has significantly advanced our understanding of health and disease. An immediate application of this knowledge base involves the development of cost-effective molecular genetic tests for more accurate diagnosis, risk assessment and prediction of response to medication. This editorial aims to introduce the family doctor to current applications of molecular genetic testing and the support systems that have been put in place in South Africa to ensure that genetic testing is applied appropriately for improved healthcare delivery and disease prevention. Practical applications of genetic research findings will be discussed in more detail in a series of articles to be published during 2005.

Genomic Medicine: Application of genomic healthcare requires the utilisation of information related to gene structure and function for risk assessment, diagnosis, and treatment of patients. Medical practitioners are in a critical position to help patients to understand the impact that genetic testing may have on their lives and the lives of their family members. It is becoming increasingly apparent that both healthy individuals and patients with disparate genetic backgrounds may respond differently to lifestyle interventions or certain medicinal agents and may even be at risk of developing drug side-effects that may be lethal. For these reasons, diagnostic and predictive genetic tests will be linked increasingly to individualised treatment response.

Genetic testing: Molecular genetic testing involves the analysis of human DNA or RNA to identify the presence or absence of specific disease-related alterations in a person's genetic material. For this purpose, a blood sample can be used or a non-invasive cheek swab sample can be conveniently collected at the doctor's practice and forwarded to the genetic laboratory for analysis. The information provided on the molecular genetic test request form by the referring doctor is used for interpretation of the test results by combining clinical, environmental and genetic factors. The findings are summarised in a confidential report, which includes guidelines for relevant treatment options or health recommendations based on all the risk factors identified.

Molecular genetic tests are used increasingly for accurate diagnosis of single gene disorders or to subcategorise polygenic or multifactorial diseases according to their genetic basis. It is likely that the focus of genetic testing will change in the near future. While family-based screening for relatively rare genetic conditions remains important, it seems inevitable that genetic testing will be increasingly performed to identify mutations of low penetrance that occur relatively frequently in the general population. This is due to the fact that nutrition and/or other lifestyle factors could determine whether persons with genetic risk factors will develop the associated disease.

A network of dieticians trained in nutritional genetics has been established countrywide (www.genecare.co.za/ Healgen.html) to provide a support base to medical practitioners who would refer patients for dietary intervention based in part on genetic test results. A question-answer service is also available and several genetic counselling facilities have been established (www.genecare.co.za/counsel.html) to assist health professionals who offer genetic testing in their practices.

What does the future hold? Genetic discoveries have led to the development of commercially available genetic tests for more than 1000 clinically-useful DNA alterations (www.geneclinics.org). As this number is expected to double over the next five years, multiplex genetic testing will replace many single gene tests. Such strip-assay tests are already available in South Africa for genetically heterogeneous diseases and complex conditions such as hereditary hemochromatosis and cardiovascular disease.[1,2] Ultimately, new micro-array technology that allows simultaneous analysis of hundreds or thousands of genes will be applied in clinical practice.

The increasing number of genetic tests that move from the research setting into clinical practice will require health care providers without specialty training in genetics to become "practitioners of genomic medicine."[3] Utilisation of the available technology will be driven by patient demand for genetic testing, which can be expected to increase significantly as test results are linked directly to key intervention strategies. By relating a person's genetic make-up with the overall risk profile a highly individualised intervention strategy becomes possible as opposed to a generalised one-size-fits-all approach. The growing support for establishment of clinical-genetic specialist networks promises to increasingly change the health system from disease management to health management. Close collaboration between molecular geneticists and primary care providers will lead to the development of educational tools and practice guidelines required for the era of genomic healthcare.

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