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HEALTH PROMOTION IN THE POST GENOMIC ERA

Preparing to Receive and Make Good Use of New Genetic Knowledge

Report of a WHO Temporary Adviser

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GENETICS WILL CHANGE MEDICINE

Knowledge is increasing rapidly in molecular and medical genetics. Within the framework of the Human Genome Initiative, genes causing disease or contributing to susceptibility to disease are constantly being cloned, mapped and sequenced. It is expected that all human genes will be mapped by year 2003-2005 and that control of gene function will soon be understood in a much more fundamental way than today. Genome-wide screening not only results in assignment of genes causing monogenic diseases, but is also useful in identifying several areas in the genome where there may be genes contributing to the etiology of common disorders such as coronary heart disease, allergies and neuro-degenerative diseases. Assignment of a clinically important gene (for example by linkage analyses of DNA markers) to a specific region of the genome, is followed by search for genes in that area and their function. The gene believed to cause disease or increased susceptibility is finally cloned and sequenced and its control is studied.

This progress will have enormous impact on clinical medicine. Diagnosis at the molecular level will be much more precise than clinical diagnosis. In complex diseases, each contributing gene will be dissected out and its effect carefully studied, also in combination with other genes as well as environmental factors. The relative importance of each gene and each environmental factor will be assessed, and the establishment of risk profiles for individuals will become feasible, based on chip technologies, or simpler methods. For many diseases, drug treatment may be tailored to the individual's risk profile. The area of pharmacogenomics is already developing, and may have a major impact on clinical medicine.

The new knowledge will make gene therapy of disorders caused by a faulty gene (loss of gene function disorder) an option for several disorders as gene delivery systems to somatic cells are improved. At the experimental level, there are already attempts being done to augment the defence systems of the body by gene therapy, to treat cancer and to prevent re-occlusion of coronary arteries following angioplasty. Newly discovered components such as angiogenesis inhibitors, or processes such as apoptosis, hold promises in the field of cancer therapy. Ways to prevent the building up of advanced glycation products or free oxygen radicals may in the future prevent or delay arterial disease and neuro-degeneration. It is work in molecular biology that points to these options for treatment or prevention, and for staying healthy even in old age.

Rapid progress in biotechnology has already led to compounds (anti-sense oligonucleotides; ribozymes) that may suppress the consequences of having a gene causing a dominant disease (gain of function disorder) or risk factor.

In 10-20 years, DNA based medicine will be in common use, and it will become possible to treat diseases where there is no therapy today. Thus, there is little doubt that human genome research and studies in clinical genetics and molecular epidemiology will greatly improve diagnostic, therapeutic and preventive work in medicine, with great benefit to patients, families and potential patients. Whereas clinical genetics 25 years ago focused almost exclusively on children and disorders of infancy, progress in genomic and other research is likely to cause a shift in emphasis towards genetic susceptibility to common diseases of middle age or old age, and towards risk reduction. The ability to predict disease risk in people who are now healthy is an important aspect of the new genetics.

GENETICS IN MEDICINE

The role of genetics in rare disorders of infancy has been appreciated for a long time. The realization that many common disorders result from the interaction between genotype and

environmental factors is much newer. Because of this important interaction, genetics and genetic risk factors have to be part of any epidemiological or public health approach to diseases and of every-day life in numerous medical disciplines.

The main clinical importance of knowledge of genetic risk factors for common disorders is that it makes it possible to identify persons at high risk who need particularly aggressive preventive measures with respect to diet, life-style and chemo-prevention.

The responsible use of genetic knowledge is to apply it only to non-directive genetic counselling, and to diagnosis, therapy and prevention, as well as related research, within a framework of voluntary testing and intervention, informed consent, respect for peoples' autonomy and privacy, and strict protection of test results.

PROBLEMS RELATED TO RISK PREDICTION

Whereas knowledge of risk for disease in the future will provide excellent possibilities to institute efficient preventive measures tailored to the individual, there are also major problems related to predictive genetic analyses.

Firstly, it may cause anxiety to learn about one's disease risk, and this could reduce quality of life. However, in families where there has been aggregation of cases of a given disorder, anxiety will often have been there for years, without the comfort derived from a negative genetic test or from careful counselling, which will always be provided with advice on risk reduction. It is an important task, however, to establish systems for risk communication that cause as little anxiety as possible and as efficient preventive, diagnostic, and therapeutic activities as possible. This work will require collaboration between several specialities and a network approach towards the individual seeking advice would be advantageous. International collaboration in developing instruments for providing risk information is called for together with initiatives to evaluate the instruments.

Secondly, knowledge that a given person has increased risk of a serious disease could be used to the tested person's disadvantage. Insurance companies, employers, prospective employers, educational institutions and credit institutions could use such knowledge in a discriminatory manner. There is a growing trend in countries with well established insurance systems towards prohibiting the use of genetic risk information for insurance purposes. This attitude is based on the notion that society should not add to the burden of those with a genetic disadvantage, for which nobody can be blamed. It is important that countries where insurance systems are now being developed are aware of this problem and make the right decisions at an early stage. In a small number of countries, use of genetic tests to a tested person's disadvantage is already prohibited by law. Broad international support for this attitude should be sought, and an understanding should preferably be reached with the insurance industry. Such an understanding could include a fixed level of health/life insurance under which insurance companies would totally abstain from considering genetic information (such an agreement was reached in Holland). Efforts towards a just insurance policy would require collaboration across disciplines.

A voluntary approach with fully informed consent and careful protection of test results are pre-requisites for predictive genetic testing.

One significant benefit of testing would be that people who turn out to not have increased disease risk may be relieved of their pre-existing anxiety.

HANDLING ETHICAL, LEGAL AND SOCIAL ISSUES

There are ethical, legal and social issues in the area of genetic testing. WHO has already worked with these aspects and should follow it up. It is crucial for achieving optimal use of genetic knowledge that these issues are handled in a responsible way and that this is made known to the public. This is particularly true for the issue of discrimination against tested persons, for example, in connection with insurance matters. No effort should be spared to reach international harmony and agreement, across disciplines. The wide-spread anxiety concerning progress in genetics makes WHO guidelines for specific procedures/situations desirable.

It is a characteristic of genetic diseases that medical information about one person could have important implications for several other persons (relatives). The family, rather than the individual is the "patient", or the unit of care. The needs for information and intervention may, under certain conditions, make it necessary to disclose genetic information to close relatives of the person seeking genetic testing and counselling. As little information as possible should be disclosed about individuals. WHO may propose rules for such "limited professional disclosure" and give advice about its implementation including the necessity to adjust laws. The justification for this would be the strong health-related needs of relatives and that it would be unfair to refuse access of relatives to information that one has oneself benefitted from. Solidarity with people with whom one shares genes and fate has a solid ethical basis. However, this area would benefit from extensive international consultation across disciplines and with lay participation where WHO could have a leading role.

Anxiety and lack of factual information could result in laws that makes it difficult to fully use genetic knowledge to promote health. WHO may consider creating and maintaining an information base where unbiased knowledge about areas in medical genetics that, by experience, often cause problems, are available.

Ethical, legal and social issues relating to medical genetics could be a field of constant WHO surveillance, as new knowledge becomes available and public opinion changes.

EDUCATING THE PUBLIC

It is being realized in several countries that public knowledge about genetics and the importance of genetics for health and disease is far from adequate. With the rapid progress in genetics, major educational efforts are needed to avoid an unacceptable information gap between lay people and professionals in the field. Such a gap could foster anxiety and suspicion, prevent people from making use of genetic services or refuse genetic treatment. Ill health could be a consequence. The inadequate knowledge is global rather than national and requires an international information strategy. Important elements would be more teaching on genetics and health in schools at all levels, improved school books, innovative educational material to the public and to schools, and correct and well presented information in media, including the Internet. People who receive genetic counselling could be equipped with educational material suitable to share with the family. Efforts must be made to increase the genetic knowledge of teachers, journalists and paramedicals, for example, in continuing education courses.

By creating and maintaining an information base on genetics, accessible to teachers, journalists, health workers and politicians, as well as the public, WHO could help secure that public opinions are based on correct, factual information. Well publicized meetings about sensitive areas or areas of misunderstanding with multi-disciplinary, as well as lay participation, could also be helpful.

DELIVERY OF MEDICAL GENETICS SERVICES and TRAINING OF PROFESSIONALS

The number of physician-geneticists will, for a long time, remain too low to cover the need for genetic counselling and genetic laboratory analyses. Several countries have not even established medical genetics as an official specialty. This should be done to ensure quality of services and WHO should play a role in advising countries at various economical and social levels how this could be achieved.

Other professionals than specialists in medical genetics must take part in the delivery of medical genetics services but they must have easy access to responsible specialists. Some countries have good experience with college-trained (two-year education) "genetic counsellors" and this trend should be encouraged. Nurses, social workers and others who have worked with patients and families could be trained over a 1.5-2 year period, under adequate supervision and "quality control", to become competent to provide routine genetic counselling following analyses of family data. There could be several such "genetic counsellors", "genetic associates" or "genetic nurses" for each physician-geneticist. WHO should assist in developing training programmes suitable for various countries.

In medical schools, genetics must be given a place that reflects its growing importance and the need to make family physicians able to conduct some genetic counselling, with the support of a regional or local center. Structures for the delivery of genetics services in a changing world should be elaborated by WHO experts.

Physicians in other specialities should have genetics as part of their training, but only in exceptional cases should they have full responsibility for genetic services. Workable solutions should be considered by WHO experts, and networks between specialities and other partnerships should be built with patients and their family in the centre.

The important roles of non-MD biochemists, molecular biologists, cytogeneticists and other professionals should be further defined by WHO experts.

Ideal and sufficient requirements to regional and local service centres should be elaborated by WHO experts. Quality control should be facilitated by WHO. WHO could maintain a database for good practices in the various fields of genetic services.

ADJUSTING REQUIREMENTS TO THE NATIONAL ECONOMY

Medical genetics services should be developed, also in countries with a difficult economy.

The careful taking of a family history should be emphasized. It is an inexpensive, yet powerful instrument in the management of families with genetic diseases. Where funds are short, an accurate family history, perhaps combined with laboratory analyses of a handful of representative members of the kindred may provide enough information for rational genetic counselling. WHO should play a role in developing useful approaches for developing countries.

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