WORLD HEALTH ORGANIZATION

EXECUTIVE BOARD **EB116/3**
116th Session **21 April 2005**
Provisional agenda item 4.1

Control of genetic diseases

Report by the Secretariat

1. Increased knowledge of genomics over the past two decades has made it apparent that the traditional category of *genetic diseases* represents only those conditions in which the genetic contribution is particularly marked, whereas in fact diseases can be arrayed along a spectrum representing the varied contribution of genes and the environment. The beneficial *applications* of genomic knowledge are still evolving, but it is expected that in the future genomics will have "a significant contribution to make to the area of public health".[1]

2. The interaction of genes with each other and with environmental factors underlies many aspects of human health and disease. However, this report focuses on the traditional category of *genetic diseases* and associated *congenital malformations*, both of which conditions are manifested early in life and for which clinical interventions are available. Genetic diseases are usually grouped into *single-gene disorders* (haemoglobinopathies, cystic fibrosis and haemophilia) and *chromosomal disorders* (Down syndrome, among others). These conditions are described as genetic diseases because a defect in one or more genes or chromosomes leads to a pathological condition. Multifactorial disorders, on the other hand, where genetic and environmental factors interact, have not traditionally been considered to be genetic diseases. Multifactorial disorders are usually categorized as *congenital malformations*, such as neural tube defect, cleft lip and palate, or *diseases with a genetic predisposition*, such as some chronic, noncommunicable diseases. In the literature, *congenital malformations* are often associated with *genetic diseases* because they both tend to present during pregnancy, at birth or in early childhood. Clinical genetics services provide care for people with both categories of disease, and registries of birth defects collect information about genetic diseases and congenital malformations. Because of their historical association, this report will consider both genetic disorders and congenital malformations.

3. Some genetic diseases, such as haemophilia, are carried on the X-chromosome (these X-linked disorders occur mainly in men). Others can arise from the presence of an abnormal gene in any autosome: if the gene is dominant, it results always in what is called a dominant condition, whereas if it is recessive many of these diseases appear only when the gene is inherited from both parents (and are thus called recessive conditions). For recessive conditions, the person who carries the abnormal gene on only one chromosome in the chromosomal pair may be unaffected or may even benefit; for instance, carriers of sickle-cell disease and thalassaemia genes may be protected from contracting malaria. This example demonstrates that environmental pressures can create reproductive advantages

[1] Resolution WHA57.13. Genomics and world health.

for carriers of a gene and make the gene more common, even though it causes a disease when inherited from both parents.

4. Genetic diseases can vary in severity, from being fatal before birth to requiring continuous management; their onset covers all life stages from infancy to old age. Those presenting at birth are particularly burdensome, however, as they may cause early death or life-long chronic morbidity. Globally, at least 7.6 million children are born annually with severe genetic or congenital malformations; 90% of these infants are born in mid- and low-income countries. Precise prevalence data are difficult to collect, especially in developing countries, owing to the great diversity of conditions and because many cases remain undiagnosed. In the developed world, genetic and congenital disorders are the second most common cause of infant and childhood death, occurring with a birth prevalence of 25-60 per 1000, with the higher figure being derived from fuller sets of data.

5. All people are at risk of diseases due to genetic mutations. The higher prevalence of genetic diseases in particular communities may, however, be due to some social or cultural factors. Such factors include a tradition of *consanguineous marriage*, which results in a higher rate of autosomal recessive conditions including congenital malformations, stillbirths, or mental retardation. Furthermore, *maternal age* greater than 35 years is associated with higher frequencies of chromosomal abnormalities in the offspring.

TREATMENT AND PREVENTION FOR THE CONTROL OF GENETIC DISEASES

6. The control of genetic diseases should be based on an integrated and comprehensive strategy combining *best possible treatment* and *prevention* through community education, population screening, genetic counselling and the availability of early diagnosis. Genetic services that are introduced for the control of genetic diseases should provide a strong platform for the application of genetic technology to a broader range of public health challenges.

7. Some of the most common genetic diseases (thalassaemias, cystic fibrosis, haemophilia and phenylketonuria) can be managed with considerable success. Effective treatment is beneficial in terms of not only increased life expectancy but also improved quality of life. Treatment and prevention are complementary and can reduce health-care expenditure, particularly in the case of common recessively inherited diseases. Also, it is hoped that the granting by national authorities of "orphan" drug designation for the treatment of rare ("orphan") diseases (muscular dystrophies and Huntington disease, for example) will encourage initiatives to promote the development of appropriate drugs and may provide therapeutic benefits to patients. In the future, somatic-cell gene therapy may play an increasing role in the management of genetic diseases, although it will take years before this becomes routine clinical practice.

8. Effective preventive approaches to genetic diseases have been demonstrated in countries where an inherited condition is common and carriers of abnormal genes can be reliably identified. For example, in Cyprus, Greece and Italy, screening for thalassaemia is standard practice and national audit data are available; most at-risk couples are identified in time to be offered early diagnosis in the first pregnancy, of whom the majority use this service and produce healthy offspring. Screening programmes need to be supported by public education and regulatory structures to empower individuals to make informed decisions and to ensure that people are protected against discrimination as a result of their test results.

GENETIC SERVICES IN PRIMARY HEALTH CARE

9. The delivery of genetic services should be integrated at all levels of health care in a way that takes full advantage of the existing resources and maximizes efficiency. The primary level of care should be the basis of all health actions in genetics, with emphasis on programmes that use simple, affordable technology and reach a large proportion of the community. Examples of actions at the primary health-care level include public education in genetics, detection of genetic risks in the community through due attention to and recording of family history in all patient encounters with the health system, premarital genetic counselling, and encouragement of reproduction at optimal maternal ages. The personnel involved in medical genetic services will most likely be primary-care practitioners with task-oriented basic training in applied genetics.

10. It is both necessary and feasible to integrate basic genetic counselling into primary health care in all countries. Genetic counselling is essential to protect the autonomy of the individual or couple and to fulfil their right to full information about the disorder and the available options. Genetic counselling must be sensitive to the cultural, religious and ethical views of the individual or couple. Central to the process of genetic counselling is its educational, voluntary and non-prescriptive nature. The main goal is that individuals facing genetic risks are impowered to make their own informed decisions, according to their own values, and then provide for these choices. Genetic counselling must, therefore, be sensitive to the roles of men and women in a community if the process is to encourage autonomous decision-making. In addition to specialized genetic counselling services, training programmes, as an integral part of patient education, should ensure that all medical staff, from nurses to physicians, are able to discuss genetic information relevant to a wide range of pathologies.

11. A barrier to implementing effective control programmes in countries is the lack of real awareness of genetic diseases and understanding of the impact of genes on health. Education in genetics is, therefore, an indispensable base on which to introduce programmes to control genetic diseases and congenital disorders. In general, countries need to improve community understanding and awareness of genetics. Furthermore, all relevant medical education and training courses should cover genetics and include modules on genetic counselling, the application of genetics to public health and the associated ethical, legal and social (including gender) issues. Countries should also aim to provide opportunities for the continuing education of their health-care professionals.

12. Other than its use in detecting a few chronic noncommunicable or infectious diseases (such as familial adenomatous polyposis and leishmaniasis), the main medical application of DNA technology is diagnosis of genetic disorders. The number of genes being identified, however, is growing rapidly and the scope of genetic diagnosis and counselling is expanding, increasing the application and importance of medical genetic services, which should become a component of health systems for all communities. Some policy-makers mistakenly believe that medical genetic services, which they associate with expensive high-technology laboratory equipment, are not a priority for developing countries. In fact, DNA diagnostic methods have become radically simplified over the past 10 years, with the latest allowing simple and rapid diagnosis. Public education and genetic counselling, as well as many genetic diagnostic tools, may be integrated into primary care even in low-resource settings.

13. Research is an important component of medical genetics. There are insufficient data currently available on the epidemiology of genetic disorders, the demand for genetic services, and the quality, use and outcomes of genetic services in developing countries. Efficient surveillance systems (registries and databases) and continued investment in genetic research are fundamental to successful public health interventions, particularly in low-resource settings.

ETHICAL, LEGAL AND SOCIAL ISSUES ASSOCIATED WITH CONTROL OF GENETIC DISEASES

14. Genomic and genetic technologies pose complex ethical, legal, social and human rights questions that are challenging numerous long-held moral assumptions. In addition, some aspects of the control of genetic diseases are closely associated with reproduction and therefore raise specific gender issues that need consideration. Also, many people with rare genetic diseases face inadequate treatment because there are few potential financial incentives for pharmaceutical companies to develop appropriate drugs. Progress is faster in the development of genetic-testing techniques than treatment. Knowledge of one's genetic status, in the absence of treatment options, may unnecessarily upset people and may place them at risk of discrimination or stigmatization. Health-care workers need to recognize and understand the sensitivity of genetic information. Genetic services need to be supported by regulatory structures that protect the privacy and confidentiality of a patient's genetic information and prevent discrimination, particularly in relation to insurance or employment. Scientific, medical and lay communities should ensure that information and technology will be used to preserve the dignity of the individual and the family. Lastly, consideration of the ethical, legal and social (including gender) implications raised by the provision of medical genetics services, and the application of their supporting genomic technologies, should be an integral part of education in genetics at all levels.

INTERNATIONAL COLLABORATION

15. WHO works with various nongovernmental organizations and Collaborating Centres that support implementation of genetics approaches to disease control in countries. Recommendations of expert groups convened by WHO over the past two decades have been implemented successfully for the prevention and treatment of haemoglobinopathies, cystic fibrosis, haemophilia, and congenital malformations in countries such as Bahrain, Belarus, Brazil, Canada, Chile, China, Cuba, Cyprus, Egypt, Greece, India, Italy, Japan, Maldives, Mexico, Nigeria, Norway, Philippines, Russian Federation, Saudi Arabia, South Africa, Sri Lanka, Switzerland, Thailand, Tunisia, and the United States of America.

PREVIOUS CONSIDERATION BY THE HEALTH ASSEMBLY

16. Although the Health Assembly has not previously discussed the control of genetic diseases, several reports to the governing bodies have examined the burden of genetic diseases and included possible prevention and control strategies for genetic disorders in the broader context of noncommunicable diseases. For example resolution WHA51.18 on prevention and control of noncommunicable diseases urged support for research in a broad spectrum of related areas, including human genetics, as a collaborative element in the development of a global strategy. The Report of the Director-General 1998-2003[1] recognized that genomics research is opening new opportunities for prevention, diagnosis and treatment. The Fifty-seventh World Health Assembly took note of the report of the Advisory Committee on Health Research on genomics and world health[2] and urged Member

[1] Document DGO/2003/1.

[2] *Genomics and world health: report of the Advisory Committee on Health Research.* Geneva, World Health Organization, 2002.

States to consider adopting its recommendations.[1] Also in response to the report, a WHO meeting on Collaboration in Medical Genetics was held (Toronto, Canada, 9-10 April 2002) to formulate a strategy relevant to WHO's country, regional and global activities in promoting genetic services and collaboration, with a special emphasis on developing countries.

ACTION BY THE EXECUTIVE BOARD

17. The Executive Board is invited to note the report and to provide guidance.

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[1] Resolution WHA57.13.