

Hereditary disorders in the Eastern Mediterranean Region

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Hereditary diseases and congenital malformations have been reported to affect 2–5% of all live births. Available evidence suggests that genetic disorders are equally important also in countries of the Eastern Mediterranean Region. Considerable achievements have been made over the last two decades in controlling communicable diseases in the region. Concurrently, there has been a mounting awareness of the increasing importance of hereditary disorders. Certain genetically determined diseases such as the haemoglobinopathies and enzymopathies are extremely common in the region and the need to initiate public health measures for their control is increasingly being recognized. The following factors may contribute to the elevated prevalence of genetically determined disorders: the high consanguinity rates; the high frequency of haemoglobinopathies and glucose-6-phosphate dehydrogenase deficiency; the trend of continuing to bear children up to menopause; the general lack of public awareness about genetic diseases; and the dearth of genetic services in the region. These and some other related issues are discussed in detail in this review article.

Introduction

Hereditary diseases and congenital malformations have been reported to affect 2–5% of all live births; they account for up to 30% of paediatric hospital admissions, and cause about half of childhood deaths in developed countries (1). Available evidence suggests that genetic disorders are important also in countries of the Eastern Mediterranean Region. For example, a survey of paediatric inpatients in a Saudi Arabian hospital from 1985 to 1989 revealed that almost 16% had congenital anomalies and genetically determined disorders (2). Furthermore, of paediatric deaths in 1985 in a Kuwaiti hospital, 37.5% were attributed to congenital heart disease and 12.5% to single-gene disorders (3).

Several factors, including those shown below, may contribute to the high prevalence of genetically determined disorders in the region.

- The high consanguinity rates, which increase the risks of recessively inherited diseases and multifactorial disorders.
- The high frequency of haemoglobinopathies and glucose-6-phosphate dehydrogenase (G6PD) deficiency, probably because of the selective advantage of carriers against falciparum malaria.

- The social trend of continuing to bear children up to menopause, which increases the predisposition to trisomies such as Down syndrome, owing to increased maternal age; also, the incidence of certain autosomal dominant disorders increases with paternal age.
- The general lack of public health measures directed at the prevention of genetic diseases and the dearth of genetic services.

Consanguinity studies

Consanguineous marriages are favourably looked upon in most Muslim countries, and consanguinity rates are high in Eastern Mediterranean countries. Table 1 shows the consanguinity rates and the rates of first-cousin marriages found in various countries in the region. The consanguinity rates range from 16.5% to 55%

Table 1: Consanguinity rates and first cousin marriages in some countries of the Eastern Mediterranean Region

| Country (ref.) | Total consanguinity rate (%) | % first-cousin marriages |
|---------------------|------------------------------|--------------------------|
| Egypt (4) | 29 | 11.4 |
| Iraq (5) | 57.9 | 30 |
| Jordan (6) | 50 | 32 |
| Kuwait (7) | 54.3 | 30.2 |
| Lebanon (8) | | |
| Christians | 16.5 | 7.9 |
| Muslims | 29.6 | 17.3 |
| Saudi Arabia (2, 9) | 55 | 31.4 |

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The rates of first-cousin marriages are closely similar (around 30%) in Iraq, Jordan, Kuwait, and Saudi Arabia. In Lebanon, the rates of consanguinity and of first-cousin marriage are higher among Muslims than Christians. Consanguinity, as defined in WHO guidelines, is a marriage between individuals who are second cousins or more closely related.^a However, some studies on consanguinity rates include marriages between third cousins. Although this discrepancy affects the total consanguinity rate, it does not markedly alter the average inbreeding coefficient. Uniformity of the definitions used in consanguinity studies is essential for making comparisons between populations. Calculation of the average inbreeding coefficient or restricting the study to first-cousin marriages are ways of increasing the reliability of investigations. It is important, also, to define the population studies in terms of religious, ethnic and socioeconomic criteria, as well as the methods used for ascertainment.

Among the offspring of consanguineous marriages worldwide, there is an increased postnatal mortality rate and an increased frequency of congenital malformation (10, 11). Several studies have been conducted in countries of the region to investigate the risks of consanguinity on reproduction (5, 8, 9, 12–15); however, because of discrepancies in the methodologies used, comparisons between the results are difficult to make. In the Islamic Republic of Iran, a study that analysed the association between consanguinity and congenital defects revealed that the incidence of major congenital malformations was 4% among the newborn of consanguineous parents, compared with only 1.7% among the newborn of non-related parents (16). Moreover, reports from Egypt and Iraq have demonstrated that the consanguinity rate among parents of mentally handicapped children was higher than that of the general population (17).^b

Consanguinity poses the most serious effects when a recessive disorder is present in the family. The chance in a first-cousin marriage of having an affected child is considerably greater than in the case of unrelated parents. Autosomal recessive disorders appear to account for a substantial proportion of physical and mental handicap in the region (18–21).^c

Despite the excess postnatal mortality associated with consanguineous marriages, there have been no reports of significant differences in the number of surviving children of marriages between related and non-related individuals. This has been explained by the higher fertility rates of consanguineous couples (22). The practice of marrying relations is unlikely to decline, and therefore genetic diseases will become more prevalent as other causes of mortality and morbidity decline (10).

Discouraging marriages between cousins is neither feasible nor desirable. However, an alternative approach is to focus on families affected by recessive conditions by establishing genetic counselling services. Such counselling must be given by experienced professionals and the response of counselled families must be evaluated. Limited experience in the region suggests that counselling on the risks of further intermarriages in families with autosomal recessive conditions is hampered by difficulties related to deeply rooted social customs and beliefs. Furthermore, considerable differences exist in the reaction of families to genetic counselling.

Congenital malformation rates

Congenital malformations arise at the time of conception or during intrauterine development, and are thus present at birth. The factors that contribute to the etiology of congenital malformations include single-gene disorders, chromosome abnormalities, multifactorial inheritance, and environmental factors.

There are considerable ethnic and geographical variations in the incidence, frequency, and distribution of congenital malformations. In developed countries such as the United Kingdom, malformations account for a substantial proportion (26–34%) of perinatal mortality (23). A similar situation is reported for the Eastern Mediterranean Region. Recent studies on perinatal mortality have drawn attention to the high contribution of congenital anomalies to perinatal deaths. A review of perinatal mortality in the Armed Forces Hospital, Riyadh, over the period 1983–87 found that 35.6% of all perinatal deaths were attributed to congenital malformations; the incidence of fatal congenital anomalies was 4.7 per 1000 births (24). Another report, from King Khalid University Hospital, Riyadh, revealed a perinatal mortality rate for the period 1982–86 of 14.5 per 1000 births, with 23% of mortalities being attributable to congenital anomalies (25).

The traditional pattern of consanguineous marriages among Arab and Muslim communities may influence the incidence of congenital malformations. Recent reports from Eastern Mediterranean countries provide useful information on the incidence of con-

^a Model education aids to assist in haemoglobinopathy control. WHO unpublished document HMG/WF/85.8a, 1985.

^b Al-Hakeem S, Hamamy H. Genetic studies on institutionalized mentally retarded males with special reference to the fragile X syndrome (Extracted from Al-Hakeem, S. Genetic studies on institutionalized mentally retarded males. MSc thesis, Al-Mustansiriyah Medical College, Baghdad, 1992).

^c Zakzouk S et al. The final report: hearing impairment among Saudi infants and children. Epidemiologic and etiologic study. King Saud University Project, 1990.

genital malformations among live births. In Benghazi, Libyan Arab Jamahiriya, a total of 33 332 children born live in the period 1982–84 were screened for easily identifiable congenital malformations. These were detected in 2.4% of all infants. Musculoskeletal malformations accounted for over a third of all the anomalies, while neural tube defects and cardiovascular anomalies represented 5% and 12% of the malformations, respectively (26).

In Bahrain, the birth frequency of congenital malformations was studied over the period 1978–85. It was found that these malformations increased in frequency from 7.24 per 1000 in 1978 to 18.5 per 1000 in 1985. Despite this considerable rise, the frequency remained within the worldwide range. Here again, anomalies of the musculoskeletal system had the highest frequency, at an average of 2.8 per 1000 (27).

Studies specifically focusing on the birth incidence of neural tube defects report various rates. In Saudi Arabia, for example, a study of 74 923 births found an incidence of 0.82 per 1000 births, while a previous study had reported an incidence of 1.6 per 1000 (28, 29). In Bahrain, Libyan Arab Jamahiriya, and Tunisia the incidences per 1000 were 1.5, 1.3, and 2.6, respectively (26–30). Throughout the world, the incidence of neural tube defects is decreasing steadily and significantly, and this trend may be valid also for some countries in the Eastern Mediterranean Region (28). Further epidemiological studies to evaluate the incidence of congenital malformations in the region are needed; special emphasis also needs to be placed on studies to verify the etiological factors involved.

Chromosomal abnormalities

Chromosomal aberrations are among the best-defined causes of congenital disease and mental handicap. At birth about 5 per 1000 liveborn children bear a chromosomal abnormality. The magnitude of this problem is difficult to define in the Eastern Mediterranean Region, because of the lack of technical resources needed to carry out such studies. In one study from the Libyan Arab Jamahiriya the incidence of all chromosomal aberrations at birth was determined to be 2.72 per 1000. This is lower than the global incidence probably because of methodological differences (26).

Down syndrome is one of the commonest chromosomal anomalies and its contribution to the etiology of mental retardation is considerable (almost 30% of cases have been attributed to Down syndrome (21)).^d The average global incidence of Down syndrome is 1.4 per 1000 of livebirths, with devia-

tions from this level being proportional to maternal age. Among live births in the region, the following incidences of Down syndrome have been reported: 1.7 per 1000 in the Libyan Arab Jamahiriya (26); 1.14 per 1000 in Bahrain (27); and 1.8 per 1000 in Egypt (31).

The factors that predispose to the non-disjunction that results in trisomy have been poorly identified, apart from the well-known influence of increased maternal age. Extrinsic factors such as biological, physical, or chemical mutagens have been implicated as etiological factors; the contribution of genetic factors and the effect of consanguinity have, however, not been clearly defined (22, 32, 33).

The contribution of chromosome aberrations to the etiology of early spontaneous abortion is well documented. Up to 50% of abortus specimens reveal chromosome aberrations, with the highest frequency being found among early pregnancy losses (34, 35). The high incidence of chromosomal anomalies among abortus material compared with that among livebirths (0.5%) confirms the power of spontaneous abortion as a tool for early elimination of defective zygotes.

Data are limited on the contribution of chromosome aberrations in spontaneous abortion in the region; however, available reports provide some useful information. A study from Saudi Arabia of 78 abortuses of 12–24 weeks' gestation reported a chromosome aberration rate of 8% (36). This comparatively low rate could have arisen because the samples were taken from abortuses after the first trimester.

The variation in the contribution of chromosome aberrations to the etiology of early spontaneous abortion may be influenced by the possible contribution of other poorly understood genetic factors. It is noteworthy that abortuses may represent lethal equivalents of single-gene disorders or multifactorial malformations, both of which could be strongly affected by inbreeding levels, which are high in the region. A recent study suggests a predisposition to spontaneous abortion in families where recurrent spontaneous abortion occurs (37).

Couples who experience recurrent fetal wastage may manifest a balanced chromosomal abnormality. Several studies, worldwide, have revealed that, on average, in 5–15% of such couples one partner is a carrier of a chromosome abnormality (38). This is of paramount importance in the context of genetic counselling and for estimating prognostic possibilities. Cytogenetic studies of couples with repeated spontaneous abortion in Qatar and Iraq have revealed a major chromosomal anomaly in one of the parents for 5.3% and 8% of the families studied, respectively (39, 40).

^d See footnote b, p. 146.

Monogenic diseases

The haemoglobinopathies and glucose-6-phosphate dehydrogenase (G6PD) deficiency are the commonest single-gene disorders encountered in the region and represent a major health problem; available data indicate that they are commoner here than in many other parts of the world. The chronic ill health and complications of these conditions pose considerable burdens on health services.

Studies on the frequency of these disorders in countries of the Eastern Mediterranean Region do not have a uniform geographical distribution. In Saudi Arabia, for example, a considerable number of studies have been undertaken in almost all the provinces. The findings provide useful information on the epidemiology of blood genetic disorders and indicate that there is a wide variability in different areas of the country. Contrasting with this situation are countries where these disorders are commonly encountered in clinical practice but for which no prevalence data are available.

Understanding about the genetic blood disorders in the region is complicated by the heterogeneity within the thalassaemia group and by the unknown interactions that occur between the different types of haemoglobinopathies and with G6PD deficiency in the same individual.

α - and β -Thalassaemias may be caused by different mutations; information about the DNA defects in a given population is valuable and helps to predict phenotypes and plan preventive measures. Molecular studies, which have been initiated in a small number of countries, need to be developed further. The main obstacle is the considerable technical requirements needed for such programmes.

Sickle cell disease

Several studies in Saudi Arabia have reported incidences of 2–27% for the carrier state for sickle cell disease and an incidence of around 1.4% for sickle cell anaemia. The highest rates are in the eastern region and the lowest in the central region of the country (41–45).

In Bahrain, sickle cell trait has been identified in 11–18% of neonates (46, 47), and sickle cell disease was reported to have an incidence of 2.1% among screened newborns.

Lower levels have been reported from the Libyan Arab Jamahiriya. In the south of the country a prevalence of 4.4% and 1.2% for sickle cell trait and sickle cell anaemia, respectively, has been found; there is considerable geographical variation in the level of abnormal haemoglobin, with the prevalence of sickle cell anaemia being only 0.005% in the east of the country (48).

Among Omani subjects, 6.1% were shown to be heterozygotes for HbA and HbS, with an estimated 3.7 homozygotes per 1000 live births (49).

β -Thalassaemia

As discussed above, the distribution of β -thalassaemia in Saudi Arabia varies according to the region. The carrier frequency lies in the range 1–15% (43, 44). In Libyan Arab Jamahiriya, the highest carrier state for β -thalassaemia has been found in the eastern region (11.2%), followed by the southern (3.2%), while the lowest is in the north-east (0.92%) (48, 50). In Pakistan, the prevalence of the carrier state has been reported to be 1.5% in Karachi and 1.6% in Rawalpindi (51, 52). The frequency of heterozygotes in Cyprus is 15–17% (53).

α -Thalassaemia

Although it was previously believed that α -thalassaemia was uncommon in the region, recent reports suggest that it is a problem of significant dimensions. Carrier state levels in the range 2–40% have been reported in Saudi Arabia and in Bahrain levels of 24.2% among neonates have been found (43, 44, 46).

Glucose-6-phosphate dehydrogenase deficiency

A total of 7.5% of the world's population carry one or two genes for G6PD, the proportion ranging from a maximum of 35% in parts of Africa to 0.1% in Japan and parts of Europe. About 2.9% of the global population is genetically G6PD deficient (54).

Although the condition is X-linked recessive, owing to the high gene frequency and consanguinity in the Eastern Mediterranean Region, homozygote females represent 10% of those who are genetically G6PD deficient. Also, 10% of heterozygote females are G6PD deficient because of unequal activation of the X-chromosome.

Several epidemiological surveys to determine the frequency of G6PD deficiency in different countries of the region have been conducted. The results confirm that the problem is a common genetic disorder. Not all countries in the region have been covered to the same extent in these surveys; in some countries, several extensive, accurate studies were performed, while in others only limited non-standardized methodologies were used.

Screening for G6PD deficiency is best performed for males only and for a certain age group. A screening test that gives the most accurate results should be used.

Table 2 shows the frequency of G6PD deficiency in different countries of the region.

Table 2: Prevalence of glucose-6-phosphate dehydrogenase (G6PD) deficiency in some countries in the Eastern Mediterranean Region

| Country (<i>ref.</i>) | % G6PD deficient (sex screened) |
|---------------------------------|---------------------------------|
| Bahrain (46) | 20.9 (both sexes) |
| Egypt (55) | 4 (both sexes) |
| Iran (Islamic Republic of) (56) | 17.88–22.8 (males) |
| Iraq (57–59) | 9–12 (males) 13 (both sexes) |
| Jordan (60) | 10 (males) |
| Libyan Arab Jamahiriya (61) | 2.5 (males) |
| Oman (49) | 27.3 (males) |
| Saudi Arabia (42, 44, 62–64) | 4.5–43 (males) |

Cystic fibrosis

Cystic fibrosis is the commonest fatal genetic disease among Caucasians, for whom the incidence reaches 1:2000. The incidence is much lower among Blacks (1:17 000) and is very rare among American Orientals (1:93 000).

The incidence levels of cystic fibrosis have recently been reported for some countries in the Eastern Mediterranean Region. The data suggest that the disease might be as common as in Europe. In Saudi Arabia, cystic fibrosis has been reported in 1:4243 children under 14 years of age (65), while in Jordan the incidence among newborns is 1:2560 (66). Cases have been reported also from the Islamic Republic of Iran, Iraq, Kuwait, Lebanon, Pakistan, and among Palestinians.

Congenital hypothyroidism

Screening for congenital hypothyroidism is now carried out in many programmes. The condition has been identified in approximately 1:3600 to 1:5000 newborns (7). Although only a few of the etiologies for congenital hypothyroidism are Mendelian, screening for this condition is commonly combined with screening of newborns for principally genetic disorders. The aim of the screening is to detect affected newborns as early as possible to permit timely management to minimize severe clinical sequelae. Screening for congenital hypothyroidism has been performed in some countries of the region and incidences among liveborn infants of 1:2666 and 1:1433 have been reported from Saudi Arabia and the Islamic Republic of Iran, respectively (67, 68).

Other monogenic conditions

Since the occurrence of genetic diseases varies widely, both geographically and ethnically, it would be

interesting to study their epidemiological pattern in the region, which is characterized by distinct ethnic groups and high consanguinity rates.

Reports from countries in the region have pointed to higher frequencies of various autosomal recessive conditions, e.g., Laurence–Biedl syndrome and multiple pterygium syndrome (prevalence, 1 per 36 000 for each in Kuwait (69)), while in Oman a prevalence of 1.2 per 10 000 live births has been reported for spinal muscular atrophies (70).

Screening programmes for monogenic disorders

Genetic diseases cause considerable human suffering and place an increasing burden on health care systems. Prevention programmes based on local circumstances should be formulated through comprehensive national plans. In some countries in the region, screening programmes for congenital diseases of newborn infants have been in effect for several decades. For example, newborn screening programmes have been initiated in Saudi Arabia and Bahrain (42, 46, 68) and have provided valuable information on the incidence of haemoglobinopathies, G6PD deficiency and congenital hypothyroidism. The aims of such programmes include the establishment of incidences for various genetic diseases and early identification of those affected in order to initiate prompt management and prevent the birth of new cases in high-risk families.

In the Aramco screening programme (42), no case of phenylketonuria was detected among 70 000 newborns screened. In Caucasians the average incidence of phenylketonuria is 1 per 10 000, and in Turkey, where the consanguinity rate is 21%, the frequency of phenylketonuria was found to be 1 per 4370 newborns (71).

Since screening during the neonatal period can be performed for several conditions, it is critical to decide, in the light of available resources and epidemiological trends, which diseases should be screened for and what are the priorities for countries of the region.

Multifactorial disorders

For many common disorders that have a familial clustering, no single gene can be held responsible; rather they are determined by many genes interacting with environmental factors. Such genetic–environmental interaction is believed to operate in the etiology and pathogenesis of hypertension, diabetes, and schizophrenia.

The prevalences of hypertension, diabetes, and coronary heart disease are growing significantly in

the Eastern Mediterranean Region. Cardiovascular diseases are now the leading cause of death in many countries of the region and available epidemiological data suggest that many of their populations have a high susceptibility to hypertension and diabetes.

Prevention and control programmes for these disorders should be based on the modification of lifestyle characteristics to prevent environmental risk factors from developing. While such programmes can be directed at the community as a whole, particularly in high prevalence areas, special emphasis should also be given to those at high risk. Identification of persons with a genetic predisposition to these disorders is therefore an important component of prevention and control programmes.

Genetic factors in infertility

A wide range of mutant genes and chromosomal abnormalities can disturb gamete formation and function in men, resulting in infertility. A significant proportion of men who are attending infertility clinics may have single-gene disorders; the higher consanguinity rates among the parents of undiagnosed cases of azoospermia in Baghdad (72) may indicate the involvement of autosomal recessive genes.

Various chromosomal disorders contribute to male infertility. Klinefelter syndrome is the most prominent of these, and accounted for 22% of azoospermic males referred to one cytogenetic laboratory in the region (72).

Female infertility may also result from chromosomal abnormalities or single-gene disorders. For example, Turner syndrome was diagnosed in 8.5% and autosomal recessive disorders in 8% of females with primary amenorrhoea who were referred for chromosome analysis in Iraq (73, 74). Also, in a study of intersexual disorders in Egypt, recessive inheritance was the predominant etiological factor (75).

Cytogenetic studies on patients with puberty problems in Tunisia revealed that 26% had chromosomal abnormalities and that 8% of infertile couples had chromosomal anomalies (76).

Cytogenetic studies of infertility should therefore be carried out in the region, with subsequent, appropriate genetic counselling.

Conclusions

- Considerable achievements have been made over the last two decades in the control of communicable diseases in the Eastern Mediterranean Region. The incidences of infections and of nutritional disorders are declining in most Member States. Concurrently, there has been a mounting awareness of the increas-

ing importance of hereditary disorders. Certain genetically determined diseases, e.g., the haemoglobinopathies and enzymopathies, are extremely common in the region and the need to initiate public health measures for their control is being increasingly recognized. Political will and national commitment at the highest level are the basic requirements for the success of prevention programmes.

- The high consanguinity rates among the populations of countries in the region constitute the most important risk factor, leading to increased prevalence of autosomal recessive conditions and possibly also multifactorial disorders. Studies of the prevalence of consanguinity in different countries are indicated. Such studies could provide essential information for evaluating the burden of genetic diseases and monitoring future trends in the region.

The impact of consanguinity on reproductive health could be investigated by studying patients with reproductive dysfunction, e.g., infertile individuals, couples with repeated fetal wastage, children with mental retardation, and infants with congenital malformations. Among the unresolved questions are the effect of consanguinity on the rate of spontaneous abortions influenced by the sharing of common antigens by the couple at the histocompatibility locus; and the effect of consanguinity on fertility.

Consanguinity studies can provide basic data on the prevalence of autosomal recessive conditions in populations. Comparison of the relative incidence of first-cousin marriages among the parents of those affected and that of the general population provides a simple method for assessing the frequency of the abnormal gene; the higher the consanguinity rate among the parents of those affected, the rarer is the condition among the general population.

Standardized methodologies and guidelines are needed to validate future comparisons between the various geographical, ethnic, and socioeconomic groups studied.

- Despite the scarcity of data, congenital malformations in countries of the Eastern Mediterranean Region appear to be occurring at rates similar to those in developed countries, and account for a considerable proportion of perinatal mortality and child morbidity.

More data are needed on the rates and types of congenital malformations in various countries of the region. Also, priority should be given to research on the major underlying etiologies and the contribution of potential environmental teratogens versus genetic factors. In the meantime, prevention programmes can be established, whenever appropriate, to focus primarily on health education, genetic counselling, and avoidance of known teratogens.

- There have been no cytogenetic screening programmes in the region to evaluate the incidence of chromosomal anomalies at birth. However, the proportion of mothers over 35 years of age is reportedly high, a factor which may predispose to increased rates of trisomies, particularly Down syndrome. Screening programmes for chromosomal anomalies are justified where resources are available. These can provide valuable information to assess the magnitude of the problem and to define future trends, taking into consideration potential environmental influences in the region.

- The haemoglobinopathies, the commonest monogenic disorder in the region, can be prevented by programmes involving health education, genetic counselling, and newborn and heterozygote diagnosis. Newborn screening for sickle cell anaemia has the advantage of early diagnosis of those affected, which is important for better management and for early genetic counselling of families at high risk. The importance of such counselling is more pronounced in countries where families tend to have large sibships.

A heterozygote screening programme for β -thalassaemia has been conducted in Cyprus. The aim was to diagnose carriers and to offer them genetic counselling and fetal diagnosis if indicated. The programme was very successful in reducing the birth rate of thalassaemia major to about 6% of that expected over a period of 15 years. Such programmes depend on advanced laboratory and obstetric technologies, with screening integrated into primary health care. The feasibility and success of such services in countries with large populations in the region should be investigated.

The complications of G6PD deficiency can be prevented by establishing screening programmes, combined with health education.

- Genetic counselling is the best practical method for minimizing the number of children born with genetic disorders and congenital malformations. This aspect of preventive medicine is just beginning to develop in some countries of the region where genetic counselling clinics have begun to function in teaching hospitals; these clinics need as much support and guidance as they can get. Expansion of such services to cover all countries of the region is urgently needed.

Prevention of genetic diseases through counselling should be established as a basic component of the medical curriculum to enable physicians in primary and higher levels of health care to deal with simple, commonly encountered genetic problems.

There is a need to promote health system research aimed at identifying appropriate approaches

and to determine the impact of genetic counselling at the primary health care level. Research should also be carried out to assess the attitudes of families towards what they learn in genetic counselling sessions and their ultimate reaction to the advice provided.

- Fetal diagnosis of genetic diseases has become an active preventive measure in developed countries. Various methods, such as chorion villus biopsy, amniocentesis, and ultrasound examination, are currently used to diagnose chromosome anomalies, single-gene disorders, and birth defects.

Cyprus is one country in the region where antenatal diagnosis is practised within the national thalassaemia prevention programme. The ethical, religious and social acceptability of this approach in other countries of the region have, however, not adequately been explored. An antenatal diagnosis service can only operate within the framework of locally adopted general guidelines on therapeutic abortion.

- Setting up computerized registers of genetically determined diseases is justified in some countries of the region. Such registers could provide valuable information about families at high risk of recurrence. The main function of the register would be to offer prospective genetic counselling to members of the population at high risk of having abnormal offspring. The systematic long-term follow-up of such registers would also facilitate monitoring genetic services as well as future epidemiological trends.

Although birth defects monitoring is a difficult task in large populations with poor record systems, in some countries of the region newborn screening for congenital malformations has provided valuable epidemiological information.

- The highly sophisticated technology linked nowadays to medical genetics should not be seen as a prerequisite to the provision of community genetic services or the initiation of genetic research programmes. Preventive strategies using simple techniques, public education, and genetic counselling can also provide valuable results.

- Even in countries with minimal resources, at least one national genetic centre should be established to provide medical services, train health professionals in the various aspects of medical genetics, and carry out research.

- Up-to-date diagnostic techniques should be introduced whenever national resources permit. These should include DNA technology and the various cytogenetic procedures for diagnosing single-gene and chromosomal disorders.

- Promotion of active collaboration, coordination and exchange of experiences between the Member

States and regional institutions and professionals concerned should be given priority in the regional Programme for Prevention of Hereditary Disorders.

Résumé

Troubles héréditaires dans la Région de la Méditerranée orientale

Les maladies héréditaires et les malformations congénitales touchent 2 à 5% de l'ensemble des naissances vivantes. Elles motivent jusqu'à 30% des hospitalisations en service pédiatrique et sont responsables de la moitié environ des décès d'enfants dans les pays développés. Contrairement à une idée reçue, il semble que les troubles génétiques soient tout aussi importants dans les pays de la Région de la Méditerranée orientale. D'après une enquête réalisée dans un hôpital d'Arabie saoudite de 1985 à 1989, près de 16% des enfants hospitalisés présentaient des anomalies congénitales et des troubles d'origine génétique. Parmi les décès d'enfants observés en 1985 dans un hôpital du Koweït, 37,5% ont été attribués à une cardiopathie congénitale et 12,5% à des troubles monogéniques.

Plusieurs facteurs peuvent contribuer à la forte prévalence des troubles d'origine génétique dans la Région, notamment: un taux élevé de consanguinité, qui augmente le risque de troubles récessifs et de troubles multifactoriels; la fréquence élevée des hémoglobinopathies et du déficit en glucose-6-phosphate déshydrogénase, probablement due à l'avantage sélectif des porteurs vis-à-vis du paludisme à falciparum; la tendance à avoir des enfants jusqu'à la ménopause, qui augmente la prédisposition aux trisomies comme le syndrome de Down, en raison de l'âge maternel élevé, tandis que l'incidence de certaines maladies à transmission autosomique dominante augmente avec l'âge paternel; et l'absence générale de mesures de santé publique axées sur la prévention des maladies génétiques, tout comme l'absence de consultations génétiques dans la Région.

Ces vingt dernières années, des progrès considérables ont été réalisés dans la lutte contre les maladies transmissibles dans la Région de la Méditerranée orientale. L'incidence des infections et des maladies nutritionnelles diminue dans la plupart des Etats Membres de la Région; parallèlement, l'importance des troubles héréditaires est de plus en plus reconnue. Certaines maladies d'origine génétique comme les hémoglobinopathies et les enzymopathies sont très répandues

dans la Région, et la nécessité de mettre en place des mesures de santé publique destinées à les combattre est de plus en plus souvent perçue.

La prévention des maladies génétiques par le conseil génétique devra être introduite dans les programmes médicales de façon à permettre aux médecins, quel que soit le niveau de soins de santé dont ils relèvent, de prendre en charge des problèmes génétiques simples mais fréquents. L'acceptabilité éthique, religieuse et sociale du conseil génétique n'a pas été assez étudiée dans l'ensemble des pays de la Région. Les services de conseil génétique ne peuvent fonctionner que dans le cadre de directives adoptées localement.

La promotion d'une collaboration active, d'une coordination et d'un échange d'expériences entre les Etats Membres, les institutions régionales et professionnels de la santé concernés devra constituer l'une des tâches prioritaires du programme régional de prévention des troubles héréditaires.

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