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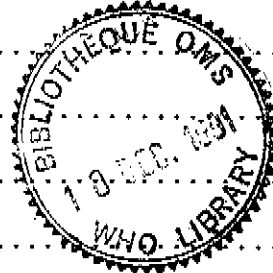
PREVENTION AND CONTROL OF CONGENITAL MALFORMATIONS IN HUNGARY

by

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## 1. INTRODUCTION

A main social target of governments, international organizations and the whole world community in the coming decades should be the attainment by all peoples of the world by the year 2000 of a level of health that will permit them to lead a socially and economically productive life<sup>1</sup>. It should include educating communities on prevalent health problems, and on methods of prevention and control. Recently congenital anomalies have become a decisive part of child health care and the right to be healthy<sup>2</sup> is an important criterion for better ways of growing up. With this in mind, an effort has been made in Hungary to integrate the so-called Optimal Family Planning Programme into primary health care as the primary prevention of congenital anomalies. Furthermore, the Hungarian Centre for Congenital Anomaly Control carries out several public health activities, such as surveillance and monitoring, diagnostic, preventive and rehabilitative activities, and acts as a health centre for congenital anomaly control including the tertiary prevention.

The term "congenital anomaly" is used by WHO in the International Classification of Diseases for the designation of structural (i.e., morphological), biochemical and functional developmental disturbances, that occur in the offspring and are present at birth whether detected at that time or not. The term congenital anomaly is a very wide one and includes a number of categories of developmental defects as follows: congenital abnormalities; genic defects including inborn errors of metabolism and chromosome aberrations; late intrauterine infections and consequent damages, the so-called fetopathies; intrauterine growth retardation; immunological disorders, e.g., mother-fetus Rhesus blood group incompatibility; mental retardation and congenital defects of the sense organs and other handicaps; and, congenital tumors.

Congenital abnormality is a structural defect that is present at birth whether diagnosed at that time or not. Recently, a pathogenesis-oriented classification has been recommended for congenital abnormalities<sup>3</sup>:

- (a) Malformation: a morphological defect of an organ, part of an organ, or larger region of the body resulting from an intrinsically abnormal developmental process, i.e., this category represents congenital abnormalities of genetic origin;
- (b) Disruption: a morphological defect of an organ, part of an organ, or a larger region of the body resulting from the extrinsic breakdown of, or an interference with, an originally normal developmental process, i.e., teratogenic and implantation disturbance factors are included;
- (c) Deformation: an abnormal form, shape, or position of a part of the body, caused by maternal mechanical forces; and,
- (d) Dysplasia: an abnormal organization of cells into tissue(s) and its morphological result(s), i.e., the process and the consequence of dyshistogenesis.

In order to develop and strengthen genetic approaches in the area of prevention related to public health problems in WHO Member States, the Hungarian experience is summarized here, and includes main principles and programme implementation aimed at the reduction of congenital anomalies at the country level.

## 2. SITUATION ANALYSIS

Hungary had a reasonably stable population of 10.6 - 10.7 million between 1980 and 1986 with an average of 135,000 births per year. The pregnancy outcomes and pathological conditions of live births are shown in Table 1.

This document concentrates upon the problems of congenital abnormalities, although similar analyses were performed for common multifactorial diseases and mental retardation<sup>5</sup>. In Hungary, congenital abnormalities are classified from several points of view. The pathogenesis-oriented one was mentioned above; here the occurrence, severity and manifestation are summarized. The occurrence per 1000 births is important from the aspect of public health and aetiology. Four subcategories: common (>1), moderately frequent (0.1-0.99), rare (0.01-0.99) and very rare (<0.01) congenital abnormalities are separated.

Congenital abnormalities can also be classified according to severity. Such distinctions are important to the clinician who must give a prognosis. Lethal abnormalities resulted in death before the reproductive age, but in general immediately after birth. In the 1980s (1980-1986), 21.9% of infant mortality was caused by congenital abnormalities in Hungary. The severe ones need urgent health care to protect life (from primary through to tertiary), and may cause "actually impaired life". The mild congenital abnormalities need medical care (e.g., surgery intervention in congenital inguinal hernia) but these do not threaten life and do not result in actually impaired life. Minor anomalies (or the recently introduced term: informative morphogenetic variants) are unusual morphologic features that are of no serious medical or cosmetic consequences to the patient - and these are excluded from the analysis because of their subjective and incomplete diagnoses. Furthermore, functional anomalies (e.g., strabismus) are also excluded. The manifestation, i.e., the pattern of structural defects, is a key factor in the pathogenesis-oriented classification of congenital abnormalities<sup>6</sup>. The isolated (single, complex - monotopic field defect, polytopic field defect and sequence) and multiple (syndrome, association and random combination) congenital abnormalities are separated. Multiple congenital abnormalities, i.e., a concurrence of two or more different morphogenetic defects in the same person are evaluated separately<sup>6</sup> and their proportion is not included into specified congenital abnormality entities (e.g., in Table 2). In Hungary there are 10 common congenital abnormalities (Table 2). All but one are isolated with a supposed multifactorial (MF) origin. The exception is Down's syndrome which is a typical multiple congenital abnormality entity caused by chromosome 21 trisomy.

The occurrences of congenital abnormalities at birth, i.e., birth prevalences have been derived from several ad hoc epidemiological studies<sup>7</sup> and from the data set of the Hungarian Congenital Malformation Registry<sup>8</sup>. The description and function of the Hungarian Congenital Malformation Registry is annexed. An attempt was made to estimate quantitatively the detriment associated with congenital abnormalities in Man<sup>9</sup>. Detriment was assessed using estimates of the years of life lost and years of potentially and actually impaired life as indicators. In these calculations it has been assumed that the average life-expectancy at live birth for the population at large is 70 years. In Hungary, the total birth prevalence of all congenital abnormalities is of the order of 600 per 10,000 ( $10^4$ ) births, i.e., it is 6% (Table 3). This includes lethal (0.5%), and severe (1.8%), [together as major congenital abnormalities (2.3%)], and mild ones (3.7%). Our calculation showed that all congenital abnormalities cause about 4900 years of life lost and about 4200 years of

actually impaired life per 10,000 live births (Table 3). Table 4 shows congenital abnormality entities of greatest importance in public health involving figures of over 100 life years lost or actually impaired life. Obviously the group of unidentified multiple congenital abnormalities, Down's syndrome, neural tube defects, congenital hydrocephaly and the different types of congenital cardiovascular malformations top this list.

There are two general areas of priority in the establishment of health objectives:

- (a) The magnitude of the problem (mortality, morbidity and disability which are expressed in terms of life years lost and actually impaired life year); and,
- (b) Technological aspects (availability and effectiveness of a technical solution).

The magnitude of the problem, i.e., the public health importance caused by congenital abnormalities is significant, due to the earliest possible onset: at birth. It explains the larger figure for life years lost and impaired life years in comparison with leading causes of death (Figure 1). Thus, the congenital abnormality "burden" is an extreme one for the human being.

The aetiological analysis of congenital abnormalities recognized from birth till the age of one year in Hungary indicated five groups:

- (a) Major genes, i.e., Mendelian entities; 6% of the total;
- (b) Chromosomal aberrations; 5% of the total;
- (c) Environmental, including teratogenic and maternal factors; 6% of the total; and,
- (d) Multifactorial aetiology; 50% of the total.

It can be inferred that about one-third of congenital abnormalities recognized at birth have no known cause at present.

Many congenital abnormalities can be prevented. Based on current estimates<sup>10</sup>, about two-thirds of all congenital abnormalities are potentially (i.e., maximum) preventable today. However, the realistic proportion of possible reduction is about 25%. The purpose of Hungarian preventive programmes is to keep offspring from getting these preventable congenital abnormalities.

### 3. OBJECTIVES AND APPROACHES

An objective generally means the end result a programme strives to achieve. In our field it is the reduction of congenital abnormalities with the help of preventive programmes based both on basic health services (such as genetic counselling and prenatal outpatient care clinics, obstetrical and neonatal-paediatric inpatient clinics) and on special primary health care approaches. Three approaches have been established in Hungary:

- (a) The Optimal Family Planning Programme;
- (b) The National Screening Programmes; and,
- (c) The Centre for Congenital Anomaly Control.

An approach essentially means a particular method of attaining an objective, e.g., to help with the use of modern methods of family planning by couples (the so-called "family planners") or the provision to identify and to devote more care to individuals who for biological, environmental or socioeconomic reasons, are at special risk of having their health impaired, of contracting a specific disease, or of having inadequate attention paid to their health problems. This strategy is known as the risk approach. The ultimate goal of a national plan of action is the establishment of a comprehensive health system, meeting all health needs of the population. Congenital abnormality prevention programmes cover measures which not only prevent the occurrence of congenital abnormalities but also arrest its manifestation, reduce its consequences once it is established, i.e., improve the quality of life of malformed children, which is often beyond the activity of the usual clinical services. Thus, in Hungary, both primary and secondary prevention programmes are used. Primary prevention seeks to avoid the causes of congenital abnormalities, thus preventing the pathogenesis of congenital abnormalities through appropriate care of the preconceptional period, and of women during pregnancy. Secondary prevention seeks to arrest the manifestation of congenital abnormalities, or to retard existing liability with the help of:

- (a) Prenatal diagnosis and, if justified, with termination of severely affected fetuses; and,
- (b) Postnatal screening programmes through early detection and appropriate treatment. (The prenataally diagnosed and terminated fetuses affected by abnormalities are also classified as secondary prevention, although this is debated by several experts, since they consider this as the manifestation of active euthanasia: "terathanasia").

In Hungary, the term "tertiary prevention" is also used for appropriate early medical treatment, psychological or other, in order to reduce the progress of the disease, and to provide rehabilitative measures. (In the case of congenital abnormalities it is better to use the term habilitation because these affected children have never had an unaffected life).

#### 4. ACTIVITIES

In order to prevent and reduce the birth prevalence of congenital abnormalities the Hungarian National Health Policy provides several programmes. Each programme has specific but different objectives. Three of these will be presented in this paper.

##### A. The Optimal Family Planning Programme

It is a voluntary health system, following an obligatory premarital medical counselling, to promote family planning, not only in the interest of prevention of unsuccessful pregnancies and congenital anomalies, but also to encourage health promotion and health protection in general. The Optimal Family Planning Programme is based on two services.

##### (a) Checking-up on reproductive health

This involves seven steps, and the four underlined have specific objectives to reduce the occurrence of congenital abnormalities in offspring. Figures mentioned are based on 5000 couples visiting our Family Planning Centre.

- Genetic background: family history. If severe monogenic or polygenic abnormalities or disorders occur in the first degree relatives of family planners, or X-linked disorders in the male relatives of female family planners, the couple is referred to the Genetic Counselling Clinic. This is necessary in 6% of the participants. Genetic counselling can reduce the risk of expected congenital abnormalities in offspring by providing counselling, prenatal diagnosis and neonatal screening to a certain extent. There is also a special "euphenic" approach within this item for the prevention of common multi-factorial disorders with late onset. However, this is not discussed in this document.
- The health condition of the female family planner: case history. Some maternal diseases (e.g., epilepsy, diabetes mellitus, thyroid disorders) require a special preconception preparation and treatment during pregnancy, e.g., the use of non-teratogenic drugs. This is done through the referral of patients to appropriate specialized outpatient clinics. Maternal diseases need expert consultation in 3% of females.
- Pregnancy fitness: special gynaecological examination. Its purpose is to detect congenital abnormalities of the female genetic organ and sexually transmitted disorders (STDs) by laboratory examination. The latter occurred in every third female and effective treatment can prevent some late complications during pregnancy.
- Male procreative fitness: voluntary sperm analysis.
- Psychosexual condition: exploration.

- Exclusion of some risk factors: voluntary blood examination. Rubella seronegative females (10% of all female participants) are vaccinated. By this approach congenital rubella syndrome is effectively prevented. (The population-based vaccination programme in infants was also launched in Hungary in 1989). The blood is used for the determination of toxoplasma and cytomegalovirus serological status in some Family Planning Centres. It is possible to ask for the AIDS test as well. So far no positive AIDS tests have been found. The prevalence of anaemia is 7%.

- Exploration of family planning wishes. If family planners want to have a baby later, appropriate contraception counselling is provided. If they want to have a pregnancy immediately, the participation in the Optimal Family Planning Service is suggested.

(b) Optimal Family Planning Service

This service is based on three principles and several methods, which may have primary preventive effect in some congenital abnormalities.

- A 3-month preparation for conception (First meeting)

. Protection of germ cells. Both females and males are asked to avoid smoking, drinking alcohol, unnecessary medication from this time on. The high compliance rate helps to prevent congenital abnormalities, e.g., fetal alcohol syndrome.

. Restoration of hormonal balance after contraceptive pills. The discontinuation of contraceptive pill usage (about 60% of couples evaluated) is suggested and condoms are provided for this period. It may prevent the low risk of congenital limb reduction deficiency caused by the periconceptual use of pills<sup>11</sup>.

. Periconceptual multivitamin supplementation. The ingestion of Elevit Pronatal<sup>R</sup> (Roche)<sup>12</sup> is launched according to a double-blind protocol in order to reduce the first occurrence of neural tube defects. The so-called "placebo" also provides useful components, i.e., Vitamin C, manganese and zinc.

. Occupational background. Occupational history. If it seems to be a risk for pregnant women and/or their fetus, an occupational doctor is asked to arrange exemption from work during pregnancy.

. Check-up and restoration of dental status.

. Beginning of specialized physical exercise.

- Achievement of conception. (Second meeting)

- . Check-up of 3-month preparation. It is satisfactory in 91% of cases.
- . The day of ovulation and the preceding day are suggested for conception.
- . Females are asked to visit the Family Planning Centre again during their first missed menstrual period.

- Protection of very early pregnancy. (Third meeting)

- . Confirmation (or exclusion) of pregnancy by a sensitive pregnancy test. Pregnancy is confirmed by ultra-sound scanning in some Family Planning Centres.
- . Avoidance of hazards to the fetus from the third week of fetal development. Thus, e.g., 3% of pregnant women need to be exempted from occupational hazards.
- . Some other protective methods are suggested, e.g., the continuation of the multivitamins till the last week of gestation, avoidance of potential teratogens, an appropriate lifestyle. Finally, pregnant women are referred to the regional prenatal outpatient care clinic.

Of course, these services are voluntary, free of charge, including the multivitamins, the rubella vaccine, the condoms, etc., and are provided by specialized nurses. These qualified nurses are community health workers who carry out this programme and they are the first who come in contact with the family planners. There is one day in each quarter for their postgraduate education, and workshops. Secondary and the rarely necessary tertiary levels of care are available for participants who are at specific risk (Figure 2).

The Optimal Family Planning Programme is a typical primary health care system which needs individual and community self-reliance and maximum community participation, that is: active involvement of people. This family planning programme implies both coordination within the health sector and intersectoral action. At the beginning of 1989, the Optimal Family Planning Programme was performed in 15 centres in Hungary; however, this number is increasing.

B. Population-based national screening programmes

In Hungary, there are four population-based prevention programmes concerned with totally or partially genetically determined congenital anomalies. All of them seek to achieve a secondary prevention.

- Maternal serum alfa-fetoprotein (MS-AFP) and ultrasonography screening. This programme involves taking a blood sample from the expectant mother at the 16th week of gestation preceded by an ultrasound examination, in order to determine exactly the gestational week. If necessary, after repeated positive MS-AFP values with negative results of repeated ultrasound scanning, an amniotic AFP examination is suggested. This programme became population-based in 1985. Both the blood examination (ELISA or RIA) and ultrasonography are performed in several health institutions.

- Prenatal chromosome examination in fetuses of mothers over 38. In the majority of cases chorionic villus sampling is performed. Amniocentesis tests are carried out at Prenatal Outpatient Care Clinics in pregnant women who are over the age of 38. There are five Prenatal Diagnostic Centres in Hungary.
- Neonatal Screening Programme. Screening of newborns for phenylketonuria (PKU) became a population-based programme in 1973. Screening for galactosemia and hypothyroidism were added later. Dried blood samples are sent to two so-called PKU Laboratory Centres.
- Orthopedic screening of neonates. The main purpose is the early detection of liability for congenital dislocation of hip. This screening is based on the Ortolani click method and some other symptoms. Suspicious cases are confirmed or excluded by X-ray examination. Of course, other congenital abnormalities (e.g., clubfoot, torticollis) are also screened by orthopedists in the Obstetrical Inpatient Clinics.

#### C. Hungarian Centre for Congenital Anomaly Control

A Centre for Congenital Anomaly Control was established in Hungary in 1973<sup>8</sup> for "disease control" and which involves all the measures designed to prevent or reduce, as much as possible, birth prevalence and the consequences of congenital abnormalities. This health centre carries out public health (surveillance and monitoring programmes), promotive (educational information booklet concerning aetiology and medical treatment of 45 congenital abnormalities, and by mass media), protective (e.g., psychological counselling at outpatient clinics for parents, mainly mothers, after unsuccessful pregnancies), diagnostic (in multimalformed babies), preventive and rehabilitative activities. All of them are based on the Hungarian Congenital Malformation Registry. The preventive and rehabilitative activities are summarized below:

- National Surveillance of Congenital Abnormalities. The Hungarian Congenital Malformation Registry has a surveillance function. There is a preliminary analysis of 45 congenital abnormality entities in each quarter based on notification received up to the 90th day after birth. The objective of this national surveillance is to detect any time or space clusters of congenital abnormalities as quickly as possible. So far two important time clusters have been found in Hungary. A temporary cluster of congenital limb reduction deficiency was detected between 1975 and 1978 indirectly caused by the officially changed population policy<sup>11</sup>. Another one was a significant increase in the birth prevalence of hypospadias from 1978<sup>13</sup>. The aetiological factors were revealed in these two clusters and it helped to prevent the higher occurrence in further years.

Other than the above-mentioned cluster-type situation, there is a continuous surveillance activity for analysis of the exposure-type situation. The consequences of epidemics are studied, e.g., rubella, influenza<sup>6</sup>; endemic environmental pollutions, e.g., air pollution, pesticide contamination, major roads; and, accident-situations, e.g., Chernobyl nuclear power accident<sup>14, 15</sup>.

- Hungarian Surveillance of Selected Congenital Abnormalities. This system is part of the International Clearinghouse for Birth

Defects Monitoring Systems<sup>16</sup>. At present 16 congenital abnormality entities and multiple congenital abnormalities are evaluated in 23 systems in 27 countries from all six continents.

- Case Control Surveillance of Congenital Abnormalities. This Surveillance was established in 1979<sup>17</sup>. It's purpose is to obtain aetiological information for the Registry immediately after the notification of congenital abnormalities in order to identify the causes (mainly, teratogens) and to assist in the prevention of further cases. However, this Surveillance is also used for primary prevention of further potentially affected sibs and the tertiary prevention of index patients. Both approaches are explained in a special booklet sent to parents within one to three months of birth after the notification of affected children. The tertiary prevention is supported by the information concerning the time-schedule of necessary treatment and an invitation to our habilitation programmes. The primary prevention of recurrence is helped by the suggestion to visit, if necessary, the genetic counselling clinic before the next pregnancy. This special booklet includes a list of these clinics. This Surveillance has a special approach and it mainly evaluates occupational background during the pregnancy of females<sup>18</sup>.

- Population Surveillance of Indicator Conditions Caused by Germinal Mutations. The main purpose is to detect the phenotypic consequences in offspring of new germinal mutations of their parents<sup>8</sup>.

- Teratological Telephone Counselling. It was established in 1985 for the whole country in order to give information concerning drug ingestion, maternal disorders, and occupational hazards during pregnancy. However, this is used for other preventive purposes too.

- Psychological counselling after unsuccessful pregnancies. This service was established in 1980 for couples, and particularly for females after the loss of fetus or infant and the birth of severely malformed offspring. The sequence of complex emotional parental reactions to the birth of an unexpected malformed baby usually involves shock, denial, sadness and anger, equilibrium and reorganization. Adequate psychological counselling can help to reduce and to shorten this pattern. It is part of the tertiary prevention and can help towards appropriate preparation for the next pregnancy.

- The Habilitation Programme of Malformed Children. This function of the Hungarian Centre for Congenital Anomaly Control helps mainly the tertiary prevention. More than 120,000 affected children are recorded in the Hungarian Congenital Malformation Registry and all surviving index patients affected by major congenital abnormalities are involved in a "habilitation" programme. This programme is based on three different age-groups:

. Parents of affected index children born in the past two years are invited for a parental meeting. Eight groups of congenital abnormalities are separated and one meeting is organized for each group per year. There are three main purposes of these meetings. First, to discuss the problems of parents and to give some

practical advice on how to care for their affected children. This information is given by several appropriate experts such as paediatricians, surgeons, psychologists, physiotherapists, etc. Second, to encourage them to establish special clubs, societies or at least personal connections, which can provide independent but joint social activity, and thus they can help one another. Third, to inform them about a special counselling section where they can obtain concrete advice for their special medical problems (e.g., how to get better prostheses for their children affected by limb reduction), other wishes (e.g., additional logopaedic education for those with oral cleft) or social difficulties (e.g., how to get the special financial support, maternity aid or prolonged child welfare, and how to improve mother-child relationship by the Gordon method).

. Affected children under 10 years of age are invited to psychological counselling to overcome a number of problems, including inferiority complexes and to improve their early development. They are also invited to participate in special courses in order to learn self-developing methods.

. Affected children over 10 years of age are invited to special counselling, where they are given advice on several subjects such as family planning, etc.

The key problem of prevention in general and particularly in congenital abnormalities is the level of health education. In Hungary there are three different systems to improve it. First, pupils in the last year of primary school (grades 1-8) and pupils in secondary schools (grades 9-12) are educated within the topic of family life. For this purpose a video-series is available which involves 5 x 45 minutes programmes (I-puberty, II-partner for life, III-birth control, IV-sexually transmitted disorders, V-family planning). Second, special information. Only two examples are mentioned here.

. There are at least three months between filing the marriage application and the marriage service. All couples receive an information booklet when they file the application.

. A special information guideline is given or sent to all couples after unsuccessful pregnancies.

Third, Hungarian mass media (TV, radio and some magazines) have permanent programmes in connection with general and special information concerning family planning and the prevention of congenital anomalies.

## 5. MONITORING AND EVALUATION

The term monitoring is used for two activities. First, the continuous follow-up of activities to ensure that they are proceeding according to plan. Second, studying a population at risk, i.e., exposed to known or suspected environmental factors (e.g., mutagens, teratogens, carcinogens). The latter is frequently confused with the term surveillance which means to study a population at large to determine the baseline occurrences of pathological conditions and to detect changes therein<sup>19</sup>.

Here the first meaning of monitoring is used and the information gained from monitoring is utilized for evaluation. Evaluation is the systematic assessment of relevance, effectiveness and impact of programmes. A programme is relevant if it answers the needs and priorities it has been designated to meet. It is effective if the results obtained are in accordance with the objectives. The impact of a programme is its overall effect on health conditions.

The main indicators of the Optimal Family Planning Programme are pregnancy outcomes (Table 5). Their occurrences are lower than expected, based on population figures (Table 1). However, it is not an appropriate comparison because of the different confounding factors. The double blind approach allows only the evaluation of periconceptual multivitamin supplementation. The total birth prevalences of congenital abnormalities were 1.7 and 2.4 per 1000 births in the study and control groups respectively, diagnosed during pregnancy or immediately after birth. Two cases with neural tube defect and one case with hydrocephalus occurred after placebo while these kinds of congenital abnormalities were not found after multivitamin use. The multivitamin use, if its effectiveness will be confirmed for the reduction of neural tube defects by the MRC Vitamin and other studies, would be very important from the practical and theoretical point of view. Obviously, the primary prevention (i.e., the prevention of pathogenesis) is better than the secondary one (i.e., the termination of malformed fetuses).

The indicators of four population-based National Screening Programmes show the virtual birth prevalences of congenital abnormalities which are screened and treated effectively. The WHO Collaborating Centre for the Community Control of Hereditary Diseases, based at the National Institute of Hygiene, is mandated to develop approaches for evaluating the relevance, effectiveness and impact of these control programmes for some totally or partially genetically determined congenital anomalies.

### (a) MS-AFP and ultrasound screening

The efficiency of this programme is not appropriate due to an ad hoc epidemiological study in patients born during 1984-1985. The proportion of false negativity was high, furthermore, some examinations were performed too late<sup>20</sup>. Since 1986, a monitoring programme has been established within the Hungarian Centre for Congenital Anomaly Control.

### (b) Prenatal chromosome examination in fetuses of mothers over 38

This programme is offered, but only one-third of eligible pregnant women were examined in 1984-1987. This is far from the desired goal. Chromosomal aberrations were found to be about 3% of fetuses studied. Monitoring is continuing.

(c) Neonatal Screening Programme

This is an effective programme. The virtual birth prevalences of PKU, galactosemia and hypothyroidism are 0.12, 0.03 and 0.23 per 1,000 live births respectively. However, nearly all cases were detected and treated, thus at present their true birth prevalences are near zero.

(d) Orthopedic screening of neonates

This programme has resulted in the almost total elimination of Hungary's most common congenital abnormalities: congenital dislocation of the hip which had a school age prevalence of 10 per 1,000 in the 1940s. However, the intensive screening frequently resulted in over diagnosis which has greatly increased the recorded birth prevalence of Ortolani positivity, i.e., the liability for this congenital abnormality. In the 1970s, 28 radiologically confirmed and treated cases were found in 1,000 babies<sup>7</sup>. In the 1980s, a new ad hoc epidemiological study was performed and it resulted in a 13.6 birth prevalence of treated congenital dislocation of the hip<sup>21</sup>.

The indicators of the Hungarian Centre for Congenital Anomaly Control vary in different functions:

(a) National Surveillance of Congenital Abnormalities

The relevance, effectiveness and impact of this programme is evaluated through the activity of the Hungarian Congenital Malformation Registry. First of all, it is measured in the disappearance of clusters. However, it also involves check-up of validity of diagnoses and the completeness of notification.

(b) Hungarian Surveillance of Selected Congenital Abnormalities

The evaluation of this programme is based on the work of the Secretariat of the International Clearinghouse for Birth Defects Monitoring Systems.

(c) Case-Control Surveillance of Congenital Abnormalities

Three types of evaluation are possible. First, an annual evaluation of the last year and of all previous data sets. Second, special detailed evaluation in connection with Hungarian problems raised by clusters or by experts living in Hungary or abroad. Third, a continuous evaluation of the validity of data by the help of special scientific approaches or by other programmes (e.g., the personal contact of index patients affected by sentinel anomalies within the Hungarian Surveillance of Indicator Conditions Caused by Germinal Mutations).

(d) Population Surveillance of Indicator Conditions Caused by Germinal Mutations

The main task of evaluation is the feasibility of this surveillance programme.

(e) Teratological Telephone Counselling

The number of telephone calls was 5,842 in 1988. Special requests are monitored concerning pregnancy outcomes. Additionally, there is a comparative analysis of telephone and personal counselling in some concrete congenital abnormality entities.

(f) Psychological Counselling after unsuccessful pregnancies

There is no monitoring for the evaluation of this service.

## 6. COSTS

The cost-benefit analysis shows the relationship between the cost of activity and the benefits accrued. Naturally, resources should be utilized as economically and effectively as possible, and the cost-benefit analysis is crucial. In general, the cost is not too difficult to estimate. The benefits, however, although often obvious, are difficult to express in those terms. The Optimal Family Planning Programme is a good example of such a case.

### A. The Optimal Family Planning Programme

The cost of different elements in the Programme is known and it is possible to calculate the cost per couple within primary health care and the extra cost including secondary health care. The benefits of the Programme were shown in the previous chapter, however, it is extremely difficult to express them in financial terms. Moreover, the benefits of the Programme extend beyond the achievement of the desired effect, i.e., reducing the occurrence of unsuccessful pregnancies, including congenital abnormalities. It may also improve the quality of life, raise productivity and self-appreciation.

The cost of primary health care per couple in Hungarian forints is 4,000 (approximately US\$80). If secondary health care is needed the cost per couple is about Hungarian forints 10,000 (approximately US\$200). Of course, the cost of manpower varies in different countries, e.g., in Hungary it is relatively low.

### B. Population-based National Screening Programmes

They are financed by the Ministry of Health and Social Welfare. The monitoring of this programme is part of the routine work of the Hungarian Centre for Congenital Anomaly Control.

### C. Hungarian Centre for Congenital Anomaly Control

The Centre is staffed by a team of seven experts: two medical doctors, a mathematician, two statisticians and two technical assistants, who work full-time in close collaboration with a group of three part-time computer experts. The budget for computer work is changing, but as an average it is about Hungarian forints 1.5 million (approximately US\$30,000).

## 7. MANAGEMENT AND OBSTACLES

It was necessary to establish a health system that will deliver management, i.e., to plan, organize, operate and evaluate all the many interrelated elements of the system. Instead of describing the management procedures as previously shown in a mosaic, its structure is illustrated in Figure 3.

The main obstacle is the difficulty to persuade couples to participate in family planning services, since it requires a profound change in the behaviour of the individual, and this is extremely difficult to achieve. Success depends on the educational level of people, e.g., the proportion of well-educated participants in the Optimal Family Planning Programme is about 50%, and their proportion is 2.5 times higher than that of the national average.

From all pregnancies the following proportion of involvement is expected in Hungary: 1989, 7%; 1990, 15%; 1991, 20%; 1992, 25-30%; 1993, 40-50%.

Population-based National Screening Programmes have different levels of effectiveness as discussed previously. The Hungarian Centre for Congenital Anomaly Control as a health centre can control congenital anomalies. The main obstacle is that it is difficult to estimate the validity of recorded data.

## 8. COLLABORATION

All these different programmes are coordinated, however, at present there are some difficulties. One problem is the coordination between experts in different fields of medicine and in other fields, e.g., sexology. Specifically and highly qualified nurses play a key role in primary health care, and they help in the coordination of different approaches. This coordination causes technical problems in secondary health care because persons at risk are treated independently.

Naturally, social and health conditions differ from country to country, and therefore the requirements for the prevention of congenital anomalies are more or less different from society to society. However, experts in all countries and societies should develop knowledge on the application of preventive measures to reduce the burden of genetic diseases, including congenital abnormalities. The international exchange of information is extremely important in order to introduce or to reorganize preventive programmes. WHO and other international bodies provide technical and managerial support, including guidelines to national, regional and global efforts.

9. **RECOMMENDATIONS**

A. Congenital anomalies do not represent a single pathological category, but comprise a number of entities which vary in their cause and natural history. Thus, there is no single strategy to prevent congenital anomalies.

B. The development of a national congenital anomaly prevention programme is not a one-time and one-approach activity. It needs continuous and multiapproach congenital anomaly control. Furthermore, these preventive programmes must be periodically re-evaluated and, if necessary, redesigned. Each country represents a special situation with its specific problems, resources and needs.

C. Of all disorder categories, congenital abnormalities, due to the earliest onset, i.e., at birth, cause the highest life years lost and the highest impaired life years.

D. Many congenital anomalies can be preventive. Based on current estimates, about two-thirds of all congenital anomalies are potentially (i.e., maximum) preventable today. The proportion of a realistic reduction estimate is about 25%.

E. All health promotion concepts, including "health for all", encompass the improvement of life-style and other social, economic, environmental and personal factors, conducive to health. However, it is worthwhile to remember one of the most important criteria of health promotion: to be born healthy.

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## A N N E X

## THE HUNGARIAN CONGENITAL MALFORMATION REGISTRY

The Hungarian Congenital Malformation Registry (HCMR) was established in 1970. The HCMR collects and maintains a computerized permanent record of medical and personal information about malformed newborns and infants born in Hungary. The study population comprises all births. The purpose of the HCMR is to determine as reliably as possible baseline figures of different types of recorded congenital abnormality (CA) entities in order to help plan medical and social services for those affected; to estimate the public health importance of different groups of CAs, so that resources can be allocated properly; to detect temporal and/or spatial changes in birth prevalences; to give adequate information in connection with public concerns (e.g., the Chernobyl nuclear plant accident); to organize population-based prevention programmes and to check the efficiency of prenatal programmes and to check the efficiency of prenatal and neonatal screenings; to help the social rehabilitation of handicapped children through special programmes; and to provide material for research projects.

The following are some special features of the HCMR.

The neonatal period, mainly the first days of life, is the usual time for diagnosis and notification\* of CAs; however, the study period covers the interval from birth to the age of 1 year. Recently, prenatally diagnosed and terminated malformed fetuses have also been recorded.

Notification of CAs is compulsory, as is the case for several infectious diseases. (In 1986, the number of infant deaths due to CAs was 45 times higher than total deaths due to infectious diseases in Hungary).

Notification is the exclusive task of physicians, mainly obstetricians (in Hungary nearly all deliveries take place in hospital) and paediatricians (who are working in obstetric inpatient clinics and various inpatient and outpatient paediatric clinics). They notify the HCMR directly, using a standard form. In case of death (stillbirths and infant deaths due to congenital anomalies) the pathologist sends a copy of the detailed autopsy record to the HCMR. Autopsy is obligatory for all infant deaths.

In addition to the multiple sources of notification outlined above, notification is made each time an affected child is admitted to any paediatric institution. Although this results in a considerable overlap, duplicate registration on the same child can be eliminated with the help of personal data. At the same time this overlap increases the efficiency of ascertainment and enhances the validity of diagnosis. Furthermore, it provides an opportunity to cross-check notifications. Failure to notify could be detected on the basis of

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\* The Term "notification" is intentionally used instead of "report" because the input of data from medical services to the HCMR is called notification while the output of data from the HCMR to medical services is called a report.

recorded data (paediatric notification forms and autopsy records provide the address of the institution where delivery took place; autopsy records include the address of the paediatric inpatient clinic where death occurred). Additionally, the observed annual total CA rate is compared with the rate expected in each obstetrical and paediatric inpatient clinic.

Submitted data (mainly diagnoses) are critically evaluated upon receipt, according to the following procedure:

(a) Forms with missing or unreliable data are sent back for completion or checking.

(b) CAs are divided into two categories: isolated (single, complex or monotopic field defect, polytopic field defect, sequence) and multiple (CA-syndrome, CA-association, unidentified multiple CAs). Distinguishing between isolated and multiple CAs is extremely important from the pathogenetic point of view, because in general, isolated CAs (e.g., cleft lip) have a more or less homogeneous origin, and probably differ for CAs that may be part of multiple entities of very heterogenous origin (e.g., the case of cleft lip as part of trisomy 13 and several other anomalies of monogenic or environmental etiology, such as EEC: Ectrodactyly - Ectodermal dysplasia - Clefting syndrome and fetal hydantoin syndromes).

(c) Minor anomalies, such as morphogenetic informative variants, and functional anomalies, such as mental retardation, must be excluded because of incomplete information and selective notification.

(d) The registry-diagnosis method is used in the case of well-known CA entities on the basis of the notified component. It means that some CAs, CA-associations and CA-syndromes are identified on the basis of predetermined criteria in the HCMR. For example, congenital cataracts and congenital cardiovascular malformations, mainly patent ductus arteriosus with or without microcephaly but without other major CAs, are diagnosed as congenital rubella syndrome, and cases with three or more VACTERL-type\* CAs without other major CAs are registered as VACTERL-association.

(e) Data are centrally coded according to the International Classification of Diseases (ICD) with certain modifications. Since ICD codes refer to isolated or single anomalies together, multiple ones are evaluated separately under a modified version of ICD rubric 759.

The unit of the HCMR is the affected individual. An index patient with two or more CAs is considered a multi-malformed person. Component CAs are coded and recorded. Thus, double registration (due to the difference between the number of anomalies and of malformed persons) can be excluded.

The deadline for receipt of data for a calendar year is 31 December of the following year. The annual report, published in May of each year, contains the following information: the birth prevalence of each CA, classified according to

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\* VACTERL - an acronym for Vertebral, Anal, Cardiac, Tracheal - Esophageal, Renal and Limb (radial type deficiency or polydactyly) used to designate a pattern of CA-association.

ICD-9 four-digit codes; the sex ratio; the outcome (still- and live births, and infant death rates); the proportion of single and multiple births; maternal age; birthweight and gestational age; the monthly and geographical distribution (20 administrative units: 19 counties and Budapest, the capital); as well as the completeness of notifications of 45 CA groups. However, a preliminary evaluation of data is made by 31 March of the following year and also published in the annual report. The difference between the birth prevalence in these two data sets is about 5-20%.

Other programmes based on the HCMR provide opportunities to check, revise, complete, and update the data base.

The recent annual total birth prevalences of CAs registered in Hungary have exceeded 47 per 1,000 total births. It is estimated that about 60 of all births per 1,000 exhibit diagnosed CA up to the age of one year. However, the birth prevalences of severe and lethal CAs are about 18 and 5 per 1,000 total births respectively, and these major CAs are nearly all ascertained.

The functioning of the HCMR is continuously checked to ensure that the following seven criteria for good registries are fulfilled:

(a) Validity of recorded diagnoses. The multiplicity of sources of notifications considerably enhances the accuracy of notified diagnoses. Additionally, the diagnoses are continuously checked through the Case-Control Surveillance System, the nationwide follow-up of multimalformed babies, the Population Surveillance of Indicator CAs, and ad hoc epidemiological studies of common and moderately frequent CAs performed by the Epidemiology Unit. These parallel activities help to limit the well-known dual effect of size, which increases statistical power and decreases accuracy. The proportion of misdiagnosis for different types of CAs ranges from 0% for cleft lip to 22% for ventricular septal defect.

(b) Completeness of ascertainment. As a result of ad hoc epidemiological studies and other programmes the approximate true birth prevalences of common, moderately frequent, and of some rare CAs are known. Furthermore, the annual evaluation of data from 20 administrative units offers another opportunity to estimate true birth prevalences, because the major cause of lower rates is incomplete notification. It should be noted that the completeness of notification also depends on the type of anomaly, e.g., it is about 100% for cleft lip but only 29% for congenital inguinal hernia.

(c) Time factor. There is an inverse correlation between promptness of notification, accuracy of diagnoses and completeness of notification. As part of the surveillance function of the HCMR, 45 CA groups are evaluated preliminarily on a quarterly basis but all CA entities are later re-evaluated in detail.

Through the Case-Control Surveillance System, several families routinely inform the HCMR about changes in the index patients' diagnosis, address, etc. In addition the Central Statistical Office provides the HCMR with information on all deaths due to CAs. The data from ad hoc epidemiological studies and other programmes are also attached to each patient's file.

(d) A pathogenetically-oriented classification. A localization-oriented anatomic classification was used previously, but an etiologically-oriented nosological classification would be ideal since information on causes is the most useful aspect. However, as the cause is still unknown for several CA entities, a reasonable compromise is a pathogenetically-oriented classification. The HCMR follows this approach.

(e) Continuous evaluation of confounding factors. Any change of pregnancy outcomes other than CAs can modify considerably the birth prevalences of some types of CAs. These confounding factors include induced abortions (mainly "therapeutic"), fetal deaths (spontaneous abortion and stillbirth), as well as low and very low birthweight. Thus, it is necessary to evaluate continuously pregnancy outcomes. In addition, some demographic variables (e.g., maternal age or differential fertility with respect to socioeconomic status) are also taken into consideration in evaluating CAs.

(f) Confidentiality of personal data. The significant circulation of confidential records related to reproduction and birth defects is causing growing public concern in many parts of the world. In Hungary, data on index patients, without personal identification, are available only to experts. Personal identification numbers, which have been used in this country since 1983, are of great help to record linkage. Additionally, a written informed consent is requested from the parents of index patients and it is obtained in 98% of cases; the names and addresses of the remaining 2% are deleted from the record.

(g) record linkage. The potential benefits of parallel evaluation of different registries have not yet been exploited. At present, only sib-occurrence is detected by this method on the basis of the maternal data.

The HCMR has helped to launch a number of projects and one of the potential benefits to be derived from this research would be a reduction in the occurrence of CAs. However, the main purpose is to promote and contribute to the improvement of medical services, and to increase the efficiency of existing preventive programmes.

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TABLE 1

DISTRIBUTION OF PREGNANCY OUTCOMES AND  
PATHOLOGICAL CONDITIONS IN LIVEBIRTHS IN HUNGARY  
1980 - 1986

Pregnancy Outcomes	%	Rate	Pathological Conditions in Livebirths	Rate
Induced abortion	34.6	-	Low birth-weight	10.02
Ectopic pregnancy	0.5	0.8 <sup>a</sup>	Congenital abnormality <sup>c</sup>	6.00
Miscarriages (spontaneous abortion)	7.2	11.1 <sup>a</sup>	Infant death	2.05
Stillbirths (late fetal death)	0.4	0.7	Mental retardation <sup>d</sup>	2.91
Livebirths	57.3	-	Blindness <sup>d</sup>	0.04
			Deafness <sup>d</sup>	0.11
<b>TOTAL</b>	<b>100</b>	<b>-</b>	Physical handicap <sup>d</sup>	<b>0.03</b>

a -  $\frac{\text{ectopic pregnancy or miscarriage}}{\text{total pregnancy - induced abortion}}$

b -  $\frac{\text{stillbirth}}{\text{still- + livebirth}}$

c - in 1977-1981, but revised birth prevalence of congenital dislocation of hip (1980-1984) and multiple congenital abnormalities (1973-1982)

d - school-age prevalence

TABLE 2

BIRTH PREVALENCE OF 10 COMMON CONGENITAL ANOMALIES, SUPPOSED AETIOLOGY, ANNUAL TOTAL YEARS LOST AND ACTUALLY IMPAIRED LIFE, HUNGARY, 1973 - 1982

ICD CODE	COMMON CONGENITAL ABNORMALITIES	BIRTH PREVALENCE PER 1000 TOTAL BIRTHS	AETIOLOGY	TOTAL YEARS LOST	TOTAL YEARS OF ACTUALLY IMPAIRED LIFE
740.0-741.0	Isolated Neural tube defect (anencephalus and/or spina bifida)	1.7	MF	621	189
745.3-4	Ventricular septal defect	1.4	MF	92	0
749.1-2	Cleft lip ± cleft palate	1.0	MF	22	141
750.5	Congenital hypertrophic pyloric stenosis	1.5	MF	0	0
752.5	Undescended testis after third month	3.6	MF	0	980
752.6	Hypospadias	2.2	MF	0	308
754.3	Liability for congenital dislocation of the hip	13.6	MF	0	10
754.5	Congenital structural talipes equinovarus	1.3	MF	0	101
550.0	Congenital inguinal hernia	11.4	MF	4	0
758.0	<u>Multiple</u> Down's Syndrome	1.2	CH	737	236

MF - Multifactorial origin  
CH - Chromosomal aberration

TABLE 3

SUMMARY OF BIRTH PREVALENCES (PER 10<sup>4</sup>), INFANT DEATH AND  
DETRIMENT ESTIMATES (PER 10<sup>4</sup>) FOR MAIN CATEGORIES OF CONGENITAL ABNORMALITIES

ICD CODE	CONGENITAL ABNORMALITIES (CAs)	BIRTH TOTAL	PREVALENCE LIVE BIRTH	INFANT DEATH %	LIFE YEARS LOST	IMPAIRED LIFE YEARS	
						POTENTIALLY	ACTUALLY
740 - 742	CAs of the nervous system	31.2	21.7	60	1,192	327	287
743	CAs of the eye	3.2	3.2	11	43	181	100
744	CAs of the ear, face and neck	4.7	4.6	0	0	322	97
745 - 747	CAs of the heart and circulatory system	80.8	79.2	27	1,839	3,722	981
745	CAs of the respiratory system	2.8	2.8	28	66	130	72
749	Cleft palate and cleft lip	14.8	14.5	3	33	982	224
750 - 751	CAs of the digestive system	27.8	27.8	21	433	1,512	69
752	CAs of the genital organs	76.6	75.2	0	0	5,264	720
753	CAs of the urinary system	17.1	15.7	6	207	892	399
754 - 756	Musculoskeletal including limb CAs	188.1	186.5	2	268	13,055	281
757	CAs of the integument	7.6	7.4	2	10	508	51
758	Chromosomal anomalies	12.6	12.6	32	313	569	560
759	Multiple*, other and unspecified CAs	37.7	33.2	18	434	1,484	390
550	Congenital inguinal hernia	114.0	114.0	0	0	7,980	-
-	Congenital tumours	1.2	1.2	5	60	24	6
<b>TOTAL</b>		<b>620.2</b>	<b>599.6</b>	<b>10</b>	<b>4,898</b>	<b>36,952</b>	<b>4,237</b>

\*Except chondrodystrophy (756.4), osteodystrophies (756.5) and chromosomal anomalies (758)

TABLE 4

LIVEBIRTH PREVALENCES AND DETRIMENT ESTIMATES PER 10<sup>4</sup> IN CONGENITAL ABNORMALITY ENTITIES WITH HIGHEST PUBLIC HEALTH IMPORTANCES

ICD CODE	CONGENITAL ABNORMALITY ENTITY	LIVEBIRTH PREVALENCE	LIFE YEARS LOST	ACTUALLY IMPAIRED LIFE YEARS
740	Anencephalus	2.0	140	0
741	Spina bifida	8.3	407	148
742.0	Congenital hydrocephaly	5.3	362	9
745.1	Transposition of great vessels	2.9	62	141
745.3	Tetralogy of Fallot	3.6	34	131
745.3-4	Ventricular septal defect	13.7	92	0
746.3-4	Aortic stenosis	5.0	143	82
749.1-2	Cleft lip ± cleft palate	10.4	22	141
752.5	Undescended testis	35.0	0	980
752.6	Hypospadias	22.0	0	308
754.6	Liability for congenital dislocation of the hip	136.1	0	10
754.5	Congenital structural talipes equinovarus	12.7	0	101
758.0	Down's syndrome	11.7	737	236
759.5-7	Unidentified multiple CAS	18.6	1,005	772

**TABLE 5**  
**PREGNANCY OUTCOMES (IN PERCENTAGE) IN THE PARTICIPANTS OF THE**  
**OPTIMAL FAMILY PLANNING PROGRAMME**

<b>GROUP</b>	<b>MISCARRIAGES</b>	<b>STILLBIRTHS</b>	<b>LIVEBIRTHS UNDER 2500g</b>	<b>MAJOR CONGENITAL ABNORMALITIES</b>	<b>INFANT DEATHS</b>
Study	9.2	0.2	5.4	1.7	0.8
Control	10.4	0.2	3.6	2.4	0.6

### Legend of figures

Figure 1. Public health importance of some leading causes of death in Hungary

Figure 2. Optimal family planning programme

Figure 3. Structure of prevention and control of congenital anomalies in Hungary

# PUBLIC HEALTH IMPORTANCE OF SOME LEADING CAUSES OF DEATH IN HUNGARY

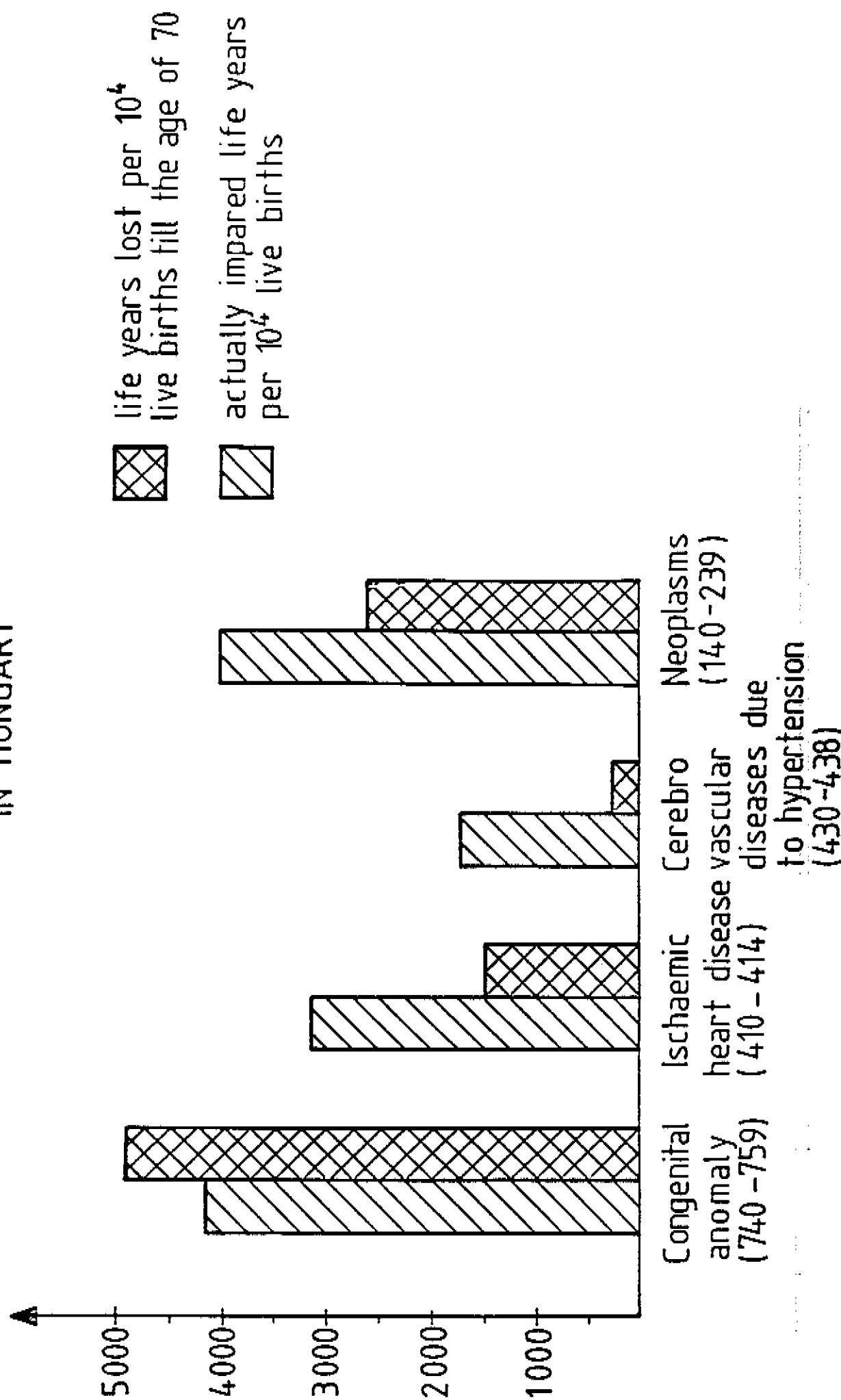
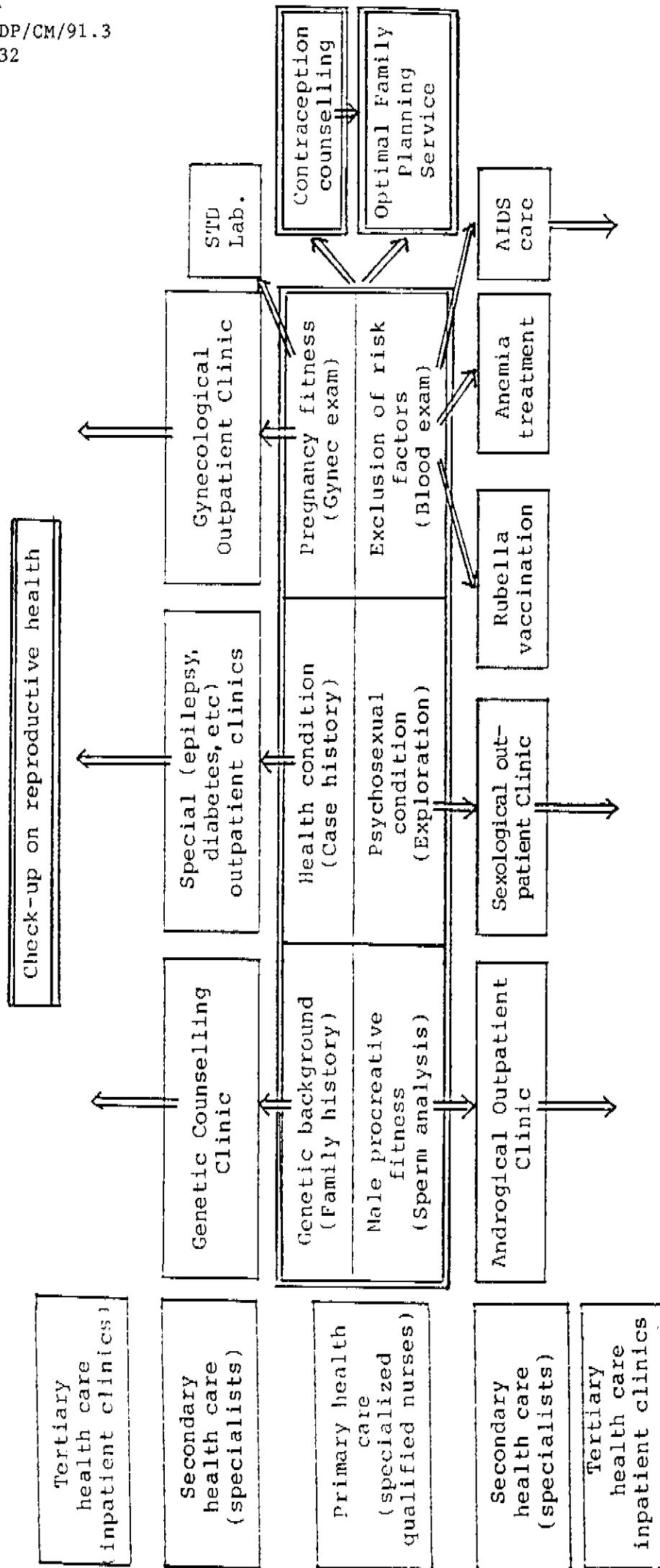
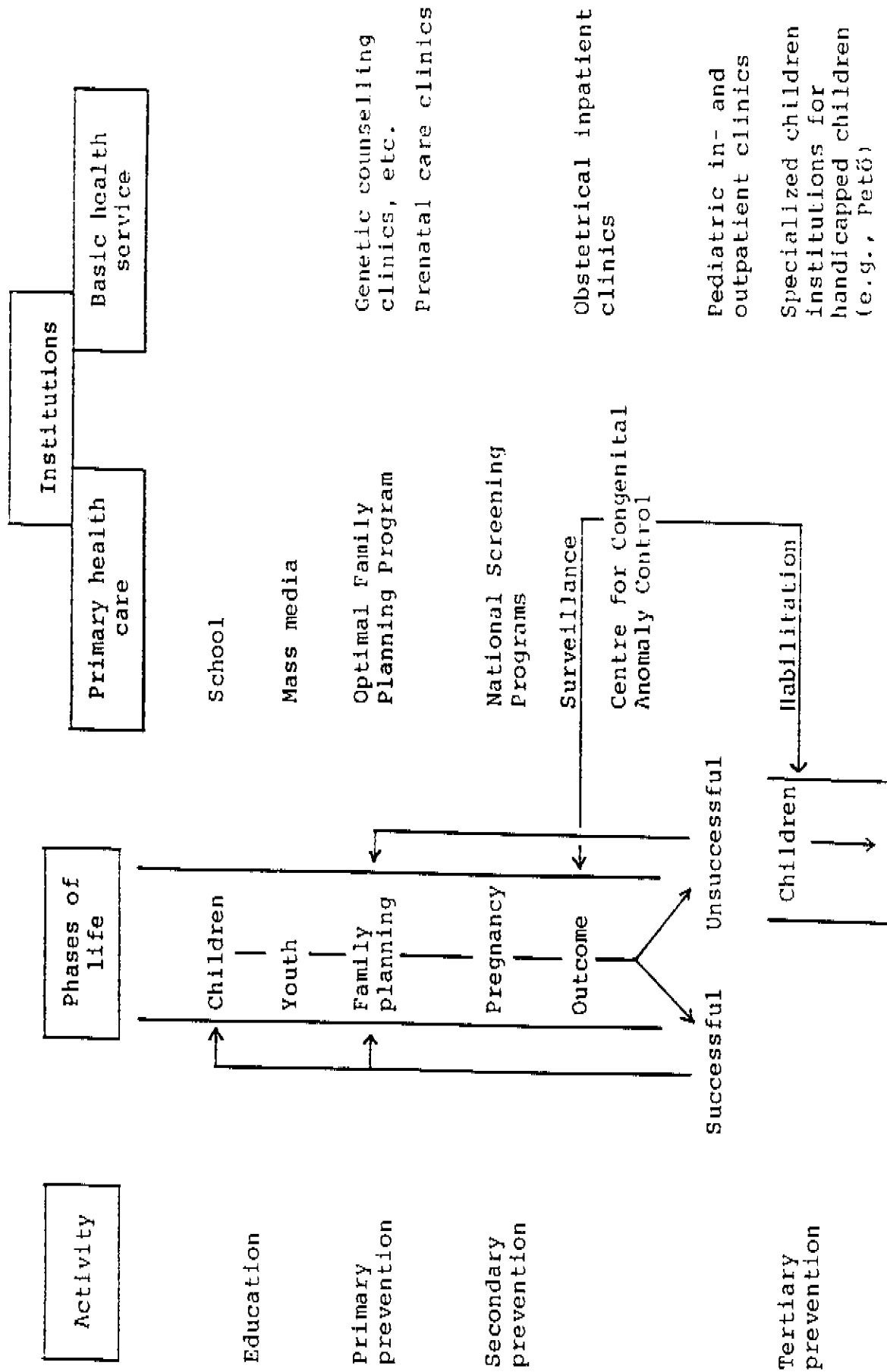


Figure 1.



OPTIMAL FAMILY PLANNING PROGRAMME

Figure 2.



Structure of prevention and control of congenital anomalies in Hungary

Figure 3.