Origin of the Polish Registry of Congenital Malformations (PRCM)

Congenital malformations as a medical and social problem

Numerous worldwide studies indicate that 2–3% of all children are born with at least one serious congenital malformation (WHO 1998; Eurocat Working Group 2002). Birth defects are also a common cause of embryonic and fetal deaths and one of the most important causes of perinatal mortality. In 1995, when the idea of a registry covering a large part of the Polish territory was conceived, the rate of perinatal fetal and newborn mortality in Poland amounted to 15.3 pro mille

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Congenital malformations were the cause of 28.6% of infant deaths, i.e., the second major cause of infant deaths (diseases of the perinatal period ranked first), and the first major cause of late (postneonatal) infant deaths (35.81%) (Brzeziński et al. 1996). In 1995, the Polish Ministry of Health launched the Programme for Improvement of Perinatal Care in Poland (Gadzinowski and Bręborowicz 1995). Soon the Programme was expanded to cover the whole country. One of the Programme’s greatest achievements was lowering of the rate of perinatal mortality to 9.4 pro mille and infant deaths to 7.7 pro mille in 2001 (Rocznik Demograficzny 2002). The Programme for Improvement of Perinatal Care in Poland, however, did not consider many aspects of congenital malformations. As the infant mortality rate was gradually lowered, the contribution of congenital malformations as causes of infant deaths increased to 34.6% of total infant mortality in 2000 (Rocznik Demograficzny 2001).

This high percentage is not the only social problem connected with congenital malformations. Children with congenital malformations require a specialist, long-term and expensive diagnosis, therapy and rehabilitation. Many morphological defects are accompanied by mental retardation. Special-care children change the functioning of the entire family and affect the quality of family life. Severe malformations accompanied by mental retardation are usually a source of deep psychological trauma and personal tragedy for the parents. In the case of children with severe congenital malformations, whose families are not able to provide proper care for them, assistance of institutions and nursing homes with qualified staff is necessary.

**Congenital malformations from the standpoint of genetic counselling**

Since the genetic factors play an important role in the aetiology of most congenital malformations, usually genetic consultation on a malformed child and, if necessary, genetic diagnosis and counselling should be offered. In Poland, in 1996, only 20% of genetic counsels, 25% of lymphocyte-based karyotype examinations, and 5% of amniocenteses were carried out, as compared with Germany 10 years earlier (1986), in relation to the number of births (source of information on the ongoing genetic care in Germany: German Society of Human Genetics, W. Vogel, personal information). The experience of Polish clinical geneticists showed that one of the reasons for such inadequate cooperation with genetic counselling clinics was insufficient knowledge of clinical genetics among general practitioners and specialists (Krawczyński et al. 1997). It is now well known that genetic counselling for the families with genetic diseases, including many families with congenital malformations, is the basic component of primary prophylaxis.

**Lack of information on the prevalence of congenital malformations in Poland**

There used to be a number of opinions in Poland concerning an increase in Down syndrome prevalence among children born to young mothers in Poland, and a more frequent prevalence of children born with congenital malformations in some regions of the country. These were intuitive opinions with no scientific support, but requiring some serious consideration. There was, for instance, no possibility of objective evaluation of the consequences of the Chernobyl disaster of 1986, including its potential impact on the prevalence rate of congenital malformations in the Polish population. Collection of data on the prevalence of congenital malformations in Poland was necessary to establish a reference point for future studies in this field and to organize healthcare programs for patients.

Before the establishment of the PRCM there were a few local registries of congenital malformations in different regions of the country. Also, there used to be some attempts to measure the prevalence of congenital malformations in Poland; however, the results were not comparable due to non-uniform data gathering systems (Kariska et al. 1976; Wołanińska et al. 1986; Mikiel-Kostyra et al. 1987). The data on congenital malformations were mostly gathered by some large specialist institutions of the Polish National Health Service. This information was of no use for epidemiological or aetiological analyses, as only selected cases of congenital malformations were registered.

In summary, there were three major reasons behind the establishment of the PRCM: (1) increasing medical and social problems associated with congenital malformations; (2) insufficient percentage of families at genetic risk that were offered genetic counselling; and (3) lack of information concerning the prevalence of congenital malformations in Poland.

**Registries of congenital malformations in the world**

Actions aimed at gradual reduction of medical and social problems connected with congenital malformations should be based on identification of all
children with malformations. Only then can the problem be fully assessed and prophylactic measures taken. Management of specialist registries is of special importance. In many countries registries of congenital malformations function as primary sources of information on the types and distribution of malformations in a given area (Eurocat Working Group 1997; WHO 1998).

Comparative studies on the incidence and types of congenital malformations in individual countries, as well as identification of possible teratogenic and mutagenic factors, require close cooperation of national registries, aimed at unification of classification criteria. For that purpose, special programs were established to incorporate the national registries, after the latter had fulfilled specified selection criteria. In Europe such an organization is the Eurocat.

EUROCAT is an EU-supported programme for epidemiologic surveillance of congenital anomalies. The objectives of Eurocat include provision of essential epidemiologic information on congenital anomalies in Europe; facilitation of early warning of new teratogenic exposures; evaluation of the effectiveness of primary prophylaxis; assessment of developments in prenatal screening; acting as an information and resource centre for health professionals, health managers, and the general population, regarding clusters of exposures or risk factors of concern; provision of a ready collaborative network and infrastructure for research on the causes and prevention of congenital anomalies and the treatment and care of affected children; acting as a catalyst for setting up registries across Europe that collect comparable, standardized data (Eurocat Working Group 2002). Eurocat Report 8 presented surveillance data from 32 registries covering a total number of 11 million births over a 20-year period (a total of 235 000 affected babies and fetuses) (Eurocat Working Group 2002). The latest Eurocat report is available at the Eurocat website (www.eurocat.ulster.ac.uk).

Polish Registry of Congenital Malformations (PRCM)

Creation and objectives of the PRCM

In 1997, the Department of Medical Genetics of the University of Medical Sciences in Poznañ received funds (after winning a competition) to establish the PRCM. From April 1997 to March 2000 the project was financed by the State Committee for Scientific Research. Thereafter, the PRCM has been continued as part of the Programme of Monitoring and Primary Prophylaxis of Congenital Malformations in Poland, financed by the Polish Ministry of Health.

The PRCM fulfils several functions, common to other birth defect registries:

– epidemiological: determination of prevalence and types of congenital malformations in the general population;
– monitoring: evaluation of the effect of the undertaken prophylactic actions, including genetic counselling, prenatal diagnosis and folic acid intake on the prevalence of congenital malformations;
– prophylactic: identification of families at genetic risk; propagation of genetic counselling among physicians and the general population; propagation of prophylactic intake of folic acid; identification of risk factors.
– socioeconomic: providing health service officials with data necessary to assess the need of medical care (diagnosis, surgery, rehabilitation, nursing homes) for children with congenital malformations;
– scientific: collection of data for scientific purposes.

Organization of the PRCM

PRCM area and population

In 1997 the organizational structure of the PRCM was devised and a database and pilot reporting to the Registry were launched. In 1998 full registration of congenital malformations was implemented. Content-related information, organizational guidelines, reporting instructions, and educational information were published in a monograph and distributed in the area covered by the PRCM (Latos-Bieleńska 1998). All the data were displayed on the Registry website (www.rejestrwad.pl).

In 1997–1998, Poland was administratively divided into 49 provinces. At that time, the PRCM covered 25 provinces, i.e. 52.9% of the Polish territory and 46.8% of Poland’s population. In 1998, the number of births in the area covered by the Registry (183 481 births) amounted to 46% of all births in Poland (Rocznik Demograficzny 1999).

In 1999 a new administrative division was instituted in Poland, and since then the PRCM covered 9 out of 16 newly established provinces. In 2000, the PRCM monitored 185 409 births
(46% of all births in Poland) (Rocznik Demograficzny 2001). In 2001, 2002 and 2004, other provinces were included in the Registry (Figure 1). Currently, the PRCM covers 85% of the Polish territory and it monitors 85% of all births in Poland (298,310 births in 2003, data for 2004 not published yet) (Rocznik Demograficzny 2004).

The PRCM Central Working Group and the computer database are located in the Department of Medical Genetics, University of Medical Sciences, Poznań. Here the collection of information, validation and analysis of data are performed.

PRCM organizational structure

The PRCM is a large registry annually monitoring from over 180,000 births (183,481 in 1998) to about 300,000 births (298,310 in 2003). The scope of the Registry requires special organization in order to obtain complete and reliable data. Its current organizational structure has resulted from many years of work of the Registry team, including management of a local registry for the Poznań Province in 1985–1997 (which was monitoring nearly 50,000 births a year), as well as from the experience of individual Registry team members in the field of healthcare organization.

At the regional level, the PRCM Provincial Working Groups have been organized. The heads of these Provincial Working Groups are leading paediatricians, neonatologists, clinical geneticists and obstetricians, heads of clinics and departments at the medical universities in Poland. The Provincial Working Groups are responsible for supervision of data collection in the province, especially active case-finding (including cases diagnosed later). Each Provincial Working Group can use the gathered data
from the province for scientific and other purposes. The PRCM staff has grown from about 250 members in 1997 to more than 400 members today. They include neonatologists, paediatricians, obstetricians, medical geneticists, paediatric surgeons, pathologists, epidemiologists, and health care organizers.

The funds of the Polish Ministry of Health received by the PRCM cover the expenses of database administration (IT service and staff), supervisory activities (inspection of reporting centres, correspondence) as well as costs of materials (notification forms, educational materials). Most activities connected with running the Registry are performed by the members of the Central and the Provincial Working Groups free of charge.

Sources of information on congenital malformations in the PRCM area

The PRCM is a population-based registry. It records data related to all births to mothers resident within the area covered by the Registry, irrespective of where the birth takes place. “Births” include livebirths, stillbirths, and rare in Poland pregnancies terminated because of severe birth defects diagnosed prenatally.

The PRCM collects information on structural defects recognized until the end of the second year of life. Most registries collect data concerning malformations recognized until the first year of life. However, some malformations of internal organs can be recognized also after this period. The experience from activities of the provincial registries and the genetic counselling clinics shows that, sometimes, a delay in psychomotor development near the end of the first year of age, which obviously draws a physician’s attention, may also reveal accompanying congenital malformations after a careful examination. Minor anomalies are excluded from registration, according to the Eurocat guidelines (Eurocat Working Group 1997, 2002). This is due to the difficulty of distinguishing between minor anomalies and normal variants as well as because of variability of reporting.

The main source of information is a double-sided registration form, developed for the Registry by the PRCM Central Working Group. For each province a different colour of registration form has been introduced. The registration forms are distributed in the Registry area, in university clinics, departments, hospital wards, outpatient clinics, and family doctor clinics.

For each child with a congenital anomaly, a detailed description of the congenital malformation is recorded. Other data include the date of birth, birth order, birth weight, gestational age at the delivery, child’s age (or gestational age) at diagnosis, parental age, education and profession, parental consanguinity, course of pregnancy, risk factors before and during pregnancy (including mother’s diseases, medication and addictions), intake of folic acid before and during pregnancy, prenatal diagnosis, family history including previous pregnancies, information whether the child was born alive, karyotype, and autopsy examination results. There are also personal data (child’s name and address), name and affiliation of the physician reporting the malformation to the Registry, and the name and address of the reporting health care institution.

Parents’ written consent is required for registration and it is accomplished through signing under a special statement on the registration form. In rare cases, when parents refuse giving the information, the malformation is reported with no personal data, but with the remaining information. Personal data is also omitted when reporting malformations identified by reviewing of birth charts only.

The registration form is filled up by the physician diagnosing the anomaly. To avoid unnecessary multiple entries, each notification to the Registry is confirmed in the child’s medical documentation and the child’s health book, with the date of reporting to the Registry. Each case-record (registration form) is sent directly to the Central Working Group at the Department of Medical Genetics in Poznañ. Case-records are updated if necessary (diagnosis of later discovered anomalies, changes or specifications in the diagnosis, etc). It is done in collaboration with specialists: clinical geneticists and cytogenetic units, cardiologists, paediatric surgeons, and pathologists.

Malformations diagnosable during the neonatal period and not reported to the Registry, are identified through reviewing birth charts by physicians from the Provincial Working Groups. It is of special importance to make sure that all malformations recognized at birth are reported to the Registry. In 1998–1999, also death and stillbirth certificates issued in the PRCM area were used as sources of additional information. A certain difficulty is witnessed in achievement of full reporting of malformations recognized after the neonatal period (about one-fourth of all congenital malformations). In such cases collaboration with various centres of paediatric care is necessary.
The encoding of congenital malformations according to the ICD-10 (Anonymous 1996) is performed by two designated (always the same) clinical geneticists from the Central Working Group. This prevents errors resulting from non-uniform encoding of some malformations.

For the entire Registry there is a single, uniform database, managed by the Central Working Group. The database is stored on an Oracle relational database server operating on the Windows NT 4.0 Server. The database is administered by a highly qualified staff from the Poznań Technical University with professional experience in management of databases for medical purposes.

Since July 2005, electronic reporting of malformations has been made possible on the PRCM website (www.rejestrwad.pl). Entries can be made by authorized physicians who can register by using access codes. After authorization and validation by a member of the Central Working Group, a notification is included in the database.

On 28 September 2005 there were 54 020 entries in the database, concerning 33 729 children with at least one congenital malformation (taking into account only the malformations reported to the Eurocat). Figure 2 presents specializations of physicians reporting the malformations. Additionally in 2004, data on a control group (children without congenital malformations) started to be gathered on a regular basis (1261 entries at present).

**PRCM as a source of identification of the families at risk**

The PRCM is an important source of identification of families at genetic risk. A list of congenital malformations has been compiled, which serves as an indication for referral to a genetic counselling clinic. Reports to the Registry are scrutinized by a clinical geneticist from the Central Working Group. Each notification is examined individually. Apart from the type of malformation also the family situation (parental age, number of children, spontaneous abortions and stillbirths in family history, congenital malformations in the other family members) are considered.

In 24% of families with a malformed child, genetic care (diagnosis and possible counselling) has been indicated as a foremost priority, and in 43% as necessary. In the case of the former, a letter is sent to such families, containing information on genetic counselling conformed to a given malformation. The counselling is not obligatory, and the correspondence is aimed at establishing contact with the genetic counselling clinic, if the family sought such professional help. The information has been sent so far to more than 6200 families, in which genetic care was indicated as a foremost priority.

Information on children with congenital malformations referred to the Registry is compared to the data from genetic clinics located in the PRCM area. It offers a unique opportunity to determine...
the demand for genetic counselling in the group of families at genetic risk.

The clinical geneticists from the PRCM Working Group can actively contact the families, if necessary, also for their own research. The PRCM was used for identification and clinical examination (also molecular studies) of children with microcephaly. Identification of children with Nijmegen breakage syndrome (NBS) has been a result of successful collaboration of the PRCM Central Working Group and the Polish NBS Registry.

**Education in the area of genetic counselling**

Education is one of the main aims of the PRCM. Education in the area of genetic counselling places a strong emphasis on the fact that clinical genetics is a significant branch of medical sciences, requiring a great deal of specialist knowledge, and that identification of genetic risk must be preceded by precise recognition of causes and calculations supported by extensive research and professional literature. General practitioners and specialists must realize that giving wrong genetic counsel can have dire and tragic consequences for all the family members.

A monograph containing data on genetic factors in the aetiology of congenital malformations, recording and interpretation of karyotype analysis results, significance of molecular studies in dysmorphology, indications of referral to a genetic counselling clinic, and diagnostic proceedings in the cases of children with congenital malformations, has been distributed in the PRCM area (Latos-Bieleńska 1998). These problems, together with information concerning clinical genetics and genetic counselling, were also published in a special issue of the Polish Journal Pediatria Praktyczna (Korman 1998). A series of 132 lectures were delivered at conferences, meetings of scientific societies, and at meetings of heads of hospital wards.

All neonatal and paediatric wards in the Registry area have been reached with instructions concerning diagnostic proceedings in the cases of children born with lethal genetic defects, if examination by a clinical geneticist is not available.

An opportunity to encourage cooperation of general practitioners, medical specialists and genetic counselling clinics has been made through contacts of the project team with numerous health service institutions in the PRCM area. These institutions include neonatal clinics and wards, paediatric clinics and hospitals, paediatric wards of general hospitals, paediatric surgery hospitals, and paediatric and specialist counselling clinics. Such contacts create excellent conditions for debate on various issues of clinical genetics, e.g. genetic factors in aetiology of congenital malformations, indications of referral to a genetic counselling clinic, indication of cytogenetic and DNA tests, storage of biological material for genetic examination, indication of prenatal diagnosis, and terms of collaboration with genetic counselling clinics. Clinical geneticists from the Central Working Group offer also consultations by phone and on the Internet.

Education of the community is an important component of medical education, aimed at raising public awareness. The aim of such education is to promote genetic counselling and folic acid supplementation. It is fulfilled with the use of mass media, and information leaflets on possibilities of genetic counselling. More than 40 lectures have been delivered.

**Achievements of the PRCM to date**

PRCM activities gave a thorough insight in the prevalence, type and distribution of congenital malformations in a significant part of Poland. It resulted in a detailed map of congenital malformations in the area covered by the PRCM. Data for 1998–1999 have been published (Latos-Bieleńska and Materna-Kiryluk 2002); data for 2000–2002 are in press.

Since 2001, the PRCM has been a member of the Eurocat. Data collected by the PRCM since 1999 have been included in Eurocat reports, available at the Eurocat website (www.eurocat.ulster.ac.uk). The updated information from the PRCM is included and identified in the Eurocat as data from the “Wielkopolska” registry (full member) and “Poland” registry (associate member). The PRCM has been participating in different Eurocat projects, e.g. folic acid supplementation (2005a; 2005b; Eurocat Folic Acid Working Group 2003).

The PRCM was a co-organizer of the 8th European Symposium “Prevention of Congenital Anomalies”, held on 9–10 June 2005 in Poznań. The abstracts of the conference papers have been published (Anonymous 2005) and can be accessed at www.rejestrwad.pl.

A number of subprojects have been undertaken: epidemiology of eye malformations, epidemiology of gastrochisis and omphalocoele, paternal age structure, ongoing genetic care for
children with congenital malformations, epidemiology of cleft lip/palate, congenital malformations in twins, etc. PRCM data served as a starting point for a pilot study on the state of medical care of children with congenital malformations. Results have been published in Polish journals and/or presented at national and international conferences.

The PRCM provides data on prevalence, type and distribution of congenital malformations for other projects and tasks (e.g. concerning environment pollution in the Silesia region, or the impact of large garbage dumps in the vicinity of human settlements on the risk of incidence of congenital malformations).

The PRCM sends an annual report to the Polish Ministry of Health and periodical reports to the provincial branches of the Polish National Health Service, on the prevalence and types of congenital malformations in the Registry area.

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