THE BEGINNINGS OF EUROCAT

A Concerted Action Project on Registration of Congenital Abnormalities and Twins in the European Community

1974-1981

by

J.A.C. WEATHERALL
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D / 1985 / 2457/24 ISBN 2-87077-308-0

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PREFACE

Epidemiology is currently defined as the study of diseases - or events pertaining to health in populations. It attempts to answer the following questions : Who is affected ? How many are they ? Where and when are they affected ? And it uses the answers to this questions to derive answers to the questions how ? and why ? Epidemiology is concerned with numbers of individuals, preferably in large enough population groups to be amenable to provide reliable statistical analysis of rates, ratios, distributions and other indices of probability. These measurements, when compared between sub-groups of a population with different characteristics or exposure to risks serve many purposes : for considering priorities in planning health services, for identifying etiological determinants of diseases, for choosing a strategy for prevention, for evaluating the effectiveness of services, for forecasting trends, for establishing surveillance systems to detect environmental risks, for analysing costs, and for studying social impacts of disease or the care thereof.

The basic information present in such indices is derived from data about individuals which are often collected in different ways by different people. It therefore calls for a common nomenclature and standard practices including methods for data-collection, terminology, diagnostic criteria and classification.

The countries, Member States of the European Community, provide an ideal ground for developing an epidemiological approach in health policy for three reasons. These countries are faced with a number of common problems, among which are the increasing exposure to environmental hazards and the spiraling increases of cost of health services. Secondly, the diversity of health care systems, styles of life, and degrees of development makes it a challenge for epidemiological studies and a great opportunity for cross-fertilization of experiences. Finally, the willingness of these countries to achieve cooperation and find solutions to their problems is an invitation for epidemiologists to collaborate. A fourth, more technical and additional, reason is that a large series of rare cases can often be assembled within a reasonably short

time span at a multinational level. This may involve a considerable saving of money and prevention of suffering. The last benefit which has become clear is the quicker development of expertise amongst staff who are often working single handed.

This book, the second of a series of EUROCAT books, presents the development of EUROCAT (European Registration of Congenital Abnormalities and Twins), one of the first Concerted Action Project of the Medical Research Programme of the European Community. The EUROCAT Project now enters its second phase, the first being concerned to develop and validate systems for the registration of congenital anomalies in a number of regions of the member states of the EEC, and to initiate monitoring of congenital anomalies in the participating centers. The second phase is to launch an effective surveillance system by analyzing trends and differences in the reported occurrence of congenital anomalies, including structural defects, chromosomal aberrations, metabolic anomalies and hereditary diseases (the first results of this second phase are published simultaneously in an accompanying book, EUROCAT no 3).

The Beginnings of EUROCAT tells of the first phase of the project (1974-1981) from its beginning till the development of a workable monitoring system, with its difficulties, its constraints, its expectation, fulfilled or not fulfilled.

The EUROCAT Project was initially conceived in 1974, at a Workshop convened by the EEC to respond to a preoccupation of CRM (Committee on Medical and Public Health Research) for improving "the methodology for population studies throughout the Community".

Before selecting the topic best suited to meet this recommendation, the meeting agreed on the long-term aim of such an undertaking, which should be to promote new attitudes toward epidemiological surveillance in the countries of the European Community. As reported in the minutes of the meeting, the project should have something which "brings the doctor in, bring the public in, has a great public health importance, is not controversial, and has great (scientific) opportunities for the future". Additional considerations of major importance were : amenability of the selected problem to preventive measures and

concrete action, educational impact, need for active participation of the medical practitioners, promotion of norms and standards at the international level.

Good choice however does not necessarily make success. It may often result in false start. One may therefore ask why EUROCAT has so fully succeeded as an exercise in European cooperation. A series of reasons might be cited to explain it; some resulting from deliberate decisions, others unexpected and fortuitous.

To the first category belong the strong interdisciplinary appeal of the study, as well as the close links between the registries and practitioners at all levels. The monitoring of congenital malformations lies at the interface between epidemiology and a number of disciplines such as genetics, obstetrics, pediatrics, neonatology, pathology, and research in microbiology, embryology, developmental biology, molecular biology, to quote only a few. This association of concerns was exploited through the organization of multidisciplinary services and training grants. EUROCAT has helped clinicians by providing guidelines for diagnosis and for classification of congenital malformations ; it has stimulated the development of paediatric cardiology and perinatal pathology ; it has supplied material for specific studies on risk factors, including risks resulting from occupational exposure. Feedback to the field personnel in charge of collecting data has proved important. However well developed during the initial phase of the project, these activities need now to be consolidated and extended.

Recent developments in some countries include relations with agencies in charge of children's welfare and associations of parents of children with anomalies, which could offer broad opportunities for education of the public.

From an organizational point of view, the most important deliberate decision was to go for regional collaboration. The registers included in the EUROCAT network - 16 in the 10 countries of the European Community at the end of the initial phase (1981), covering over 200,000 births per year - were provisionally selected by two consultants, with the help of national contacts,

during a two-year feasibility study which included a survey of existing resources and visits to potential participants. The main criteria used in the selection were interested motivation of individuals, resources (occasionaly the existence of a local register), and the possibility of collecting population-based data. The final proposal, with one or two exceptions, was endorsed by governments who incidentally approved commitment to funding at the national level (EUROCAT being a Concerted Action, which means that the Commission provides funds exclusively for coordination, while local funding is the responsibility of national governments).

In retrospect, this somewhat peculiar regional structure has ensured a unique spirit of cohesion within and collaboration between registers which work together in the project. One disadvantage could be that local registers do not always have the required capacity to serve as a nucleus for extending registration to the remainder of the country, which is one of the long-term objectives of the project. Also, in spite of their official commitment, some governments may not always fully comply to provide the necessary funding of proposed registers which appear to be the result of personal initiatives rather than a national undertaking.

This flexible regional structure, which has proved efficient and rewarding, has been achieved at a time when the Commission was embarking on its first large-scale Medical Research Programme and a number of rules of procedure had still to be invented and codified.

EUROCAT has also taken advantage from a scientific and technological conjuncture which has developed beyond all expectations. In the large majority of the ten member states, prenatal diagnosis is becoming a routine procedure. Analysis of the trends after birth of those malformations which can be detected before birth is essential to evaluate the use of pre-natal preventive services. In the field of biomedical engineering, echography is undergoing a tremendous expansion, which calls for a reassessment of its potential for diagnosis. Recent advance in developmental biology (such as the identification of parental non-disjunction in trisomy 21) calls for studies based on

appropriately collected epidemiological data. Finally, a growing concern for the long term effects of environmental hazards, including occupational risks, for which congenital anomalies constitute one of the most early warnings, call imperatively for the monitoring of large series of well-validated population-based data to serve as baselines for surveillance.

One of the major achievements of EUROCAT has been to develop throughout the countries of the EEC, a common language for epidemiological surveillance in a most complex field such as the congenital anomalies, while respecting the particular practices within each country. It thus demonstrated that the diversity of health systems is not an insuperable obstacle for carrying out joint epidemiological studies and setting up a common surveillance system. Obvious difficulties due to different methods of data-collection within different administrative contexts by different types of personnel can be circumvented by using precise definitions, harmonizing data-collection methods, and standardizing diagnostic criteria, characteristics of the population, and types of information to be collected.

It has also proved that statistical data collected for epidemiological purposes can be transmitted across national borders with full respect to all rules pertaining to data-security and protection of confidentiality.

The EUROCAT in its initial phase has provided the testing ground for these activities whose importance for the health of the population will only grow in the future years. Of no lesser importance, it has led to the development of a tool for services and research in a field of great concern for the individuals in the community and for the family, for which the birth of a handicapped child is an unmitigable tragedy.

This development has been made possible thanks to the help and foresight of the European Community, the Committee for Medical and Public Health Research (CRM), and its subworking group on Epidemiology, Biostatistics and Clinical Trials.

It would however not have been developed without the dedication and expertise of all involved in the day-to-day work, the Registry Leaders and their staff as well as the staff at the Central Registry in Brussels, under the undaunted leadership of Dr. Josephine Weatherall, to whom due tribute has to be given. EUROCAT in some ways is her offspring. It is now ready to grow up and gradually to embark on surveillance activities.

Michel F. LECHAT

FOREWORD AND ACKNOWLEDGMENTS

First and foremost the author wishes to thank Professor Michel F. LECHAT for his help at all times. Without his imagination and determined resourcefulness EUROCAT would not have been created.

In preparing this brief account of the development of one of the multicentre research projects coordinated by the E.E.C. as part of its first medical research program, the author has attempted to present to the public some taste of the excitements and frustrations in the early days of cooperation between nine independent European countries.

The author has been much assisted in the study by Dr. K. GERBAULET and the staff of DGXII and for permission from the E.E.C. to reprint tables from "Illustrated guide to malformations of the central nervous system" by Professor Norman C. NEVIN and Dr. J.A.C. WEATHERALL.

The author also wishes to acknowledge with thanks the help given by Dr. Hector FOWLIE, Dr. Elizabeth RUSSELL, Dr. André BAERT in their help with the planning and preparation of this history.

Thanks are due too to Dr. M.A. BLEIKER and to Dr. G. DEAN for their help with planning the study and in carrying it out.

Finally the author wishes to thank the Registry Leaders, and their local supporting staff, the staff of EUROCAT central office and the staff of the Department of Epidemiology at the Catholic University of Louvain in Brussels, who have all assisted in the development of EUROCAT in many ways. Particular thanks go to Ms. Dominique MOUSSET who has patiently and carefully prepared many drafts of the text and the final copy.

P A R T 1

THE START OF A MEDICAL RESEARCH PROGRAM IN THE E.E.C.

1.1. Introduction

EUROCAT (European Registration of Congenital Abnormalities and Twins) is the acronym given to one of the three Concerted Action Projects of the First Medical Research Programme of the European Community. The three projects, 1) Cellular ageing and decreased functional capacity of organs; 2) Extracorporeal Oxygenation; 3) Registration of Congenital Abnormalities were initiated in 1978 but the development to this point took about five years, as is outlined in the rest of this chapter.

1.2. Development of Medical Research within the Community.

When the Treaty of Rome was signed in 1957 it aimed "to lay foundations of an enduring and closer union between the European peoples by gradually removing the economic effects of their political frontiers"... To some extent these aims overlapped the older foundation, the Council of Europe, which was founded in 1949 with the aim of achieving "greater unity between its members, to safeguard their European heritage and to facilitate their economic and social progress". This Council has in effect been the birth place of the now elected European Parliament which shares with the Council of Ministers a supervisory rôle over the recommendations of the European Commission. The interaction and precise rôles of the several bodies which are working towards a well integrated set of independant European States, is difficult to comprehend but this is not the place to attempt an explanation.

Collaboration in medical research in Europe, mostly related to public health, was already taking place during the 1960's on the recommendation of the Committee of Partial Agreement in Public Health which met under the auspices of the Council of Europe. Various collaborative exercises had been carried out through committees of consultants. For example, the European Pharmacopoeial Commission and the Council of Europe published Vol. 1 of the first edition of the EUROPEAN PHARMACOPOEIA in 1969. Other tasks such as reviewing deaths from lung cancer or accidents and the listing of laboratories concerned with the screening of new borns for inherited metabolic diseases have been sponsored by the Council of Europe. In 1966 a group of Experts in Classification of Malformation was

invited to make recommendations for the classification and surveillance of congenital malformations.

Other medical research projects have been for many years coordinated by the European Regional office of the World Health Organisation in Copenhagen, Denmark. Studies from this office have extended to volunteer countries in both East and West Europe, each country's effort being financed through local finances (either from private research funds or from national research bodies) with the coordination and some of the costs of analysis and conferences paid for from World Health Organisation funds.

The Treaty of Rome however contains no specific statements about collaboration in medical matters, but interest in medical matters within the scope of the treaty has come from several directions : from the field of social policy : from interest in the health and protection of a healthy environment for all Europeans : from the opportunities available to migrant workers or to handicapped persons. It is however in the field of Science and Technology that the Medical research programs, of which EUROCAT is one, have developed.

Cooperative activity in the field of Scientific and Technological research within the European Commission was started in 1965 when a working party "Politique de Recherche en Science et Technologie" (PREST) recommended a "need for coordination of national scientific and technical interests" with the objectives of developing new methods to monitor, to control and to improve the safety of the European environment : to promote the use of newly developed techniques for medical care and to stimulate the manufacture of new instruments. A "Study group in medical research related to public health" consisting of experts from Member States was invited to assist "PREST" in forming a strategy on the medical research aspects of its policy. The group met during 1971 and 1972. It chose to follow "the principle research objectives :

- prevention;
- early diagnosis of disease;
- rehabilitation"

and particularly to choose methods and themes in which scientific and technological progress bring a benefit to medical care.

The group highlighted topics for high priority in medical research as follows :

1. Metabolic and psychosomatic factors in cardiovascular diseases.
2. Environmental and genetic factors in respiratory diseases.
3. Psychosomatic, metabolic and environmental factors in digestive diseases.
4. Embryotoxic, genetic and environmental factors in congenital disorders.
5. Psychological, physiological and metabolic aspects of ageing.
6. Psychological toxic and environmental factors in road traffic accidents

and gave advice on implementation of these recommendations through three ad-hoc specialist groups, and a supervisory committee of people responsible for national research organisations. The very comprehensive report, was approved by a Summit Conference in Paris in October 1972, as a result of which a first meeting of the supervisory committee - the Committee for Medical Research (CRM) took place on 11th December 1972.

The Committee for Medical Research (CRM).

The CRM is a body of national delegates in Medical Research which advises the Committee for Recherche en Science et Technology CREST (which replaced PREST in 1973). For all these advisory Committees the Commission provides secretarial services and transmits any advice from the committees to appropriate persons or committees within the Commission.

The recommended terms of reference which CRM were given by PREST for its first meeting included the consideration of "the importance of cooperation in medical research within the European Community... directed towards preventive medicine and rehabilitation : the development and dissemination of new medical techniques particularly in the fields of epidemiology, medical biology and bio-medical engineering".

At the first four meetings of CRM during 1973 the main discussions concerned the aims of research and the methods by which the objectives set by CREST could be attained. The priorities and criteria for the selection of projects were, as already stated, to concern the prevention of illness and disability, and the early detection of disease and rehabilitation. It was agreed that research should be performed within the existing research organisation of member states : should be of importance to the community : should have practical importance, especially from a social and economic point of view and should be more effective on a community basis than within any single member state. A further stated objective was to "encourage coherence of methods of working of the national research organisations thus laying the foundations for an effective scientific community" although this was recognised to be difficult in the prevailing context.

At the 5th Meeting of CRM in November 1973 a proposal concerning the methods by which the CRM should act to further medical research in the community was put forward by the Chairman.

CRM 's rôle in research should be of coordination, and of making full use of the research organisations or agencies in each country thus avoiding potential conflict between the EEC coordinated activities and provision of local funds. About the discussion of these proposals the minutes of the meeting reported..."There should be no problem provided that the CRM procedures are such that the timing of decisions allows the necessary consultations to be held". These proposals were the basis of research by "Concerted or Common Action" in the first and second medical programmes.

1.3. The Special Working Groups.

By the end of the first quarter of 1973, CRM had established the three Specialised Working Groups A- in Medical Biology, B- in Biomedical Engineering and C- in Epidemiology, Statistics and Clinical Trials along

with two further ad-hoc working groups to guide research on (a) psychological, toxic and environmental factors in road traffic accidents and (b) deafness, including the harmful effects of noise and giving particular attention to the effects of congenital disorder.

During the summer of 1973 the Specialized Working Groups (SWG) were starting to work. They were composed of an expert and a "reserve expert" in each specialisation appointed by each of the nine member states.

The members present at any one such of committees meeting should therefore have amounted to nine representatives from member states. In fact this composition for the SWG Epidemiology was rarely achieved. Some members consistently sent two representatives to meetings, others sent none.

The terms of reference of these Specialised Working Groups appear to be more extensive than any group has in practice yet achieved. Objectives such as "the dissemination of information on methodology with particular reference to techniques applicable in population studies" sound more like a policy for the editor of a publishing journal. However "the preparation of proposals for projects" seems more in line with what has been achieved. In fact, the special working groups have been moderately successful in this context. Most Groups had their first meeting late in 1973 or early in 1974.

1.4. The work of the Specialized Working Group in Epidemiology.

The first meetings of the SWG in epidemiology (SWG EPID) took place in April and June 1984 their proceedings out are poorly documented. During these meetings general objectives and methods of working were settled as described by Professor Lechat in the preface, and several favoured topics emerges of which malformations was one. Members were encouraged to explore the interests in their own countries.

Already by May 1974 Professor M.F. Lechat of the Catholic University of Louvain in Brussels had organised a research group of persons interested in congenital abnormalities in Belgium and this group was put forward to

other members of the SWG EPID as an example of appropriate national initiative. It is notable that Prof R. Beckers of the Belgian Ministry of Health who initiated in West Flanders one of the first systems for registration of malformations at birth in Europe and had also been a member of the group advising the Council of Europe since 1966, became a member of this Belgian group.

By June 1974 four projects developed by the SWG EPID were put forward to CRM and CREST - namely :

1) An inventory of epidemiological research in the E.E.C.
2) Promotion of teaching in epidemiology
3) Specific training in epidemiology
4) A seminar on congenital malformations

and by September 1974 CRM and CREST had approved that Prof. Saracci and Prof. Lechat should organise a Seminar on Congenital Malformations.

Other projects being developed at the first meeting were a review of health surveys in the Community and studies in the epidemiology of old age.

1.5. Contemporary developments in the study of birth defects.

The climate of thought during the 1960's and early 1970's was becoming more concerned with birth defects and their prevention. Many countries had been affected by the increase in the number of surviving babies with gross limb anomalies consequent on the use of thalidomide as a sedative in early pregnancy between 1958 and 1962, and in many countries, legal actions against the manufacturers were being fought out in the courts.

Paediatric surgeons during the 1960's were carrying out operations to promote the survival of infants with spina bifida, many of which had incurably abnormal development of their brain and spinal cord. Parents of such handicapped children had started to question the benefits of such treatment.

By the late 1960's many countries had established systems for monitoring defects observed at birth : others had instituted longitudinal studies in search of etiological factors.

In 1966, the World Health Organisation (W.H.O.) published the results of a world wide survey of about 5500 babies born with birth defects observed at birth occurring in a total of about 427,000 births recorded consecutively in hospitals in 16 countries between 1961 and 1964 (Stevenson et al. 1966).

The study showed that defects of similar types were occurring in most countries, and that frequencies for the commoner malformations observed at birth showed distinct differences between centres. However, as the study was based on hospitals and therefore on a potentially selected group of births, comparisons of incidence of defects in the local populations should be made with caution.

In 1970 the secretariat of W.H.O. reconsidered whether the W.H.O. should recommended any further studies in the recording of birth defects and a group of consultants prepared a paper reviewing the types of data collection suitable for various types of study (W.H.O. 1970). The report clearly differentiated two types of study. One involved keeping a register of every child or person living in a defined location in whom a congenital abnormality was discovered - no matter at what age. Such a register can provide population based estimates of the frenquency of occurrence of all kinds of birth defects. The second type aims to notify quickly the malformations discovered at birth and concentrates on the conditions which are recognisable at that age. Such a system provides as early as possible data for quick detection of increases in the defects recognised, which could be caused by some adverse environmental factor.

A second and larger consultation held in 1972 reviewed the earlier advice, pointed out that there were already about 19 centres round the world which were recording defects at birth and advised that WHO should take up a rôle of coordinating these studies in order to have a centralised and sensitive "collaborative reporting system for the monitoring of malformations" (W.H.O. 1972).

In 1958, the charitable organisation "The National Foundation - March of Dimes", founded in 1938 to unify the fight against poliomyelitis and having largely completed this task, turned to the challenge of "Birth Defects". It organised conferences in 1960 in London, in 1963 in New York, in 1969 in the Hague and in 1973 in Vienna (Motulsky et al 1974). As a result of recommendations made at the latest of these International Conferences, the National Foundation - March of Dimes decided to sponsored a meeting in 1974 of persons in charge of systems for recording defects at birth, a sponsorship which led eventually to the establishment in 1975 of the International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS) which has met, annually since. This Clearinghouse which has by 1984 grown into an independent "Non Governmental Organisation" or "International Association", collates and disseminates quarterly reports of information from each of the data systems from about 16 countries each of which collects data on certain birth defects known to be easily observed at birth or discovered immediately after birth. The "Clearinghouse" also undertakes some epidemiological investigations of variations in levels of reporting observed in one or more of the cooperating areas.

1.6. Development of a Study in Congenital Abnormalities by members of the SWG EPID.

The workshop of invited experts which Professor Lechat had been authorized to organise, took place in Brussels on November 18-19th 1974, and it was attended by representatives from 8 out of the 9 member states, with observers from Norway and the WHO European Region, as well as three members of the EEC Commission (Appendix Ia). The title and terms of reference were "Epidemiological Monitoring in the countries of the European Community, taking congenital malformations as a model".

The preliminary requisites of the topic to be selected were therefore stated as follows :

(1) there is hope for prevention and/or treatment ;
(2) it is useful on a community-wise basis ;
(3) there is a good chance to achieve demonstrable results ;
(4) the decision-makers, the public, and the medical profession are sensitive to the topic ;

(5) it should have an educational value in promoting new attitudes.

The participants had to decide between two broad types of studies, i.e. a limited area of investigation, implying ad hoc surveys or the use of existing data for testing a given hypothesis, or a multi-purpose data collection system. The setting-up of a data collection system for congenital anomalies was a compromise, which apparently met all of the above criteria. It proved an excellent choice. The rest of the story is to be found in this book.

In discussion about monitoring of congenital malformations it was recognised that already the National Foundation - March of Dimes had taken an initiative to start coordinating any systems which were recording defects recognisable at birth. However, as many important defects are not detected until later in infancy, a study which would collect and monitor accurate and complete data on a population basis for all malformations was seen to be needed to validate and supplement the reporting from the studies which measure only the "point prevalence" of defects detected at birth. The meeting ended by recommending three topics for further consideration : "a selective register for congenital malformations", "a register of children with inherited biochemical abnormalities" and "a long-term study of twin registers".

The report of this meeting was favorably received by the SWG EPID at its next meeting, and Prof. Lechat was authorized to hold a further smaller meeting to draft a final protocol for a cooperative study on congenital malformations and inherited abnormalities in the countries of the EEC (Appendix Ib). This meeting took place on March 24th 1975 and the report was presented to the SWG EPID and then to CRM by June 1975.

1.7. A Feasibility Study.

CRM received the report of the working group and immediately commissioned a feasibility study. 10,000 units of account were allocated and it was agreed that the study should be undertaken by Dr. Geoffrey Dean and Prof. M.F. Lechat.

The first study was a conference in September 1975 with Professor Krohn at the University of Odense in Denmark at which the establishment of a register in the island of Fünen in Central Denmark was discussed. Such a register was evidently feasible without substantial changes in the methods of data collection but the funding of staff to operate such a register was evidently not locally available.

Following the visit to Denmark, Professor Lechat and/or Dr. Dean visited or met with representatives from many centres in Europe which were either already engaged in the recording of birth defects or were wishing to establish such a study. In visiting some centres they were accompanied by additional observers (Appendix Ic).

The final feasibility report was presented to CRM as an appendix to a "proposal for a common action in the field of Congenital Abnormalities" on June 30th and July 1st 1976 (XII/591/76 E).

1.8. Time of commissioning a Study.

Between July and October 1976 there was evidently considerable correspondence between the secretariat of the Commission and the research departments of the member states, and the next appearance of the study was its presentation as a draft proposal for a First Medical Research Program to CRM (DG XII/859/76 E) on 7-8th October 1976.

There followed a delay of almost a year before semi-official steps towards the implementation of "Common Action Studies" were taken. The reasons for this delay appeared to be the slow passage of the proposals through the various and many committees of the Commission and the Council of the E.E.C. as summarised in the following table.

Calendar of procedures which has been involved in adoption of the 1st Medical Research Programme.

Commission :	-	preparation of draft proposal	: November 1976
	-	consultation and opinion of CRM	: December 1976
	-	consultation CREST	: January 1977

- internal procedures : consultation of other Directorates General, translation in 6 languages, approval by Commission
- submission to Council : June 1977

Council :
- transmission for opinion to CREST, European Parliament and Social Committee of the E.E.C. : June 1977
- CREST opinion : July 1977
- European Parliament : opinion of
  - Committee on Environment, Public Health and Consumer Protection : October 1977
  - Committee on Budgets : October 1977
  - Plenary Session : November 1977
- Economic and Social Committee adoption of opinion in plenary session : November 1977
- Council's internal procedures :
  - Working Party on research : January 1978
  - Committee of Permanent Representatives : February 1978
  - Adoption : February 1978

Although the proposal passed smoothly through the various committees, it was impossible at the time to be sure that this would happen and therefore it wasn't until December of 1977 that the way was seen to be clear enough for the Commission to authorize a Workshop to finalise a working program for the study.

In the absence of official approval it is not surprising that Member States had made little, if any, preparation for financing the study in their own countries.

1.9. An unofficial Start.

The delay was to some extent shortened by a workshop held in January 1978 organised by the secretariat of the EEC and Professor Lechat and approved by CRM, with the objective of finalising the working program for the study.

Persons invited to this workshop were those who were expected to be leading the study groups in each country mentioned in the proposals approved by CREST. In many cases it became apparent that the studies which had been reviewed in the feasibility study of 1975-1976 were not the same as those which the Member States wished have included in the study. However the meeting was attended by 21 persons representing potentially 13 registers, one or more in each of the nine members states. The meeting was also attended by a representative from the EEC, by Professor Lechat, by the Project Leader designate and her assistant.*

During the two days of discussion, agreement was reached about objectives, methods, and priorities, which were sufficient to allow the Project Leader, when officially appointed, to start to plan the work of coordination. It was agreed that cases born on or after the first of January 1979 would be included in the study.

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* Members of Working Group on Congenital Malformations : EUROCAT Preliminary Conference - January 23-24 1978.
Belgium : R. Beckers, Ministry of Health, I. Borlée, UCL, M.F. Lechat, UCL, R.F. Vlietinck, KUL and P. De Wals, UCL.
Denmark : M.M. Hauge, University of Odense, P. Howitz, Ministry of Health, and S. Sorensen, Minsitry of Health.
France : J. Feingold, I.N.S.E.R.M., and C. Rumeau-Rouquette, I.N.S.E.R.M.
United Kingdom : G.D. Forwell, Greater Glasgow Health Board, F.M.W. Hamilton, Greater Glasgow Health Board, F. Harris, University of Liverpool, N.C. Nevin, University of Belfast, and J.A.C.Weatherall, Office of Population, Censuses and Surveys.
Grand-Duché of Luxemburg : C.E. Rischard, Ministry of Health.
Ireland : G. Dean, Medico-Social Research Board, and P. Kirke, Medico-Social Research Board.
Italy : C. Galanti, Tuscany Department of Health and Social Security, and M. Marchi, Biostatistics Unit of CNR.
Netherlands : W.M.J.Van Duyne, Ministry for Public Health and Hygiene.
Federal Republic of Germany : K.H. Degenhardt, University of Frankfurt, and G. Simon, Statistical Bureau of Hesse.
E.E.C. : L. Karhausen.

P A R T I I

THE EUROCAT PROJECT IN THE E.E.C.

2.1. Introduction

Although many persons who were likely to become involved with a study in malformations in the Member States were identified by the time of the official approval in February 1978, many of the existing registers were unable to start to obtain extra finance for the new activities from national or regional research funds until the project had been officially approved. In some countries the decisions about the existence and whereabouts of a registry were delayed till this point.

It also became apparent that a study of the registration of twins and multiple births, which had earlier been suggested as an independent project in the SWG/EPID, had been added to the proposal to register congenital abnormalities.

2.2. Supervision of the Study.

The report of the Council Decision of February 13th 1978, which set up the first three Concerted Action Projects in the First Medical Research Program of the European Economic Community , includes details of the objectives of the study and how it would be supervised. The text also provides for the supervision of the study : "A concerted action committee for each project would be established" which would have the following terms of reference :

" 1.1. contribute to the optimum execution of the programme by giving its opinion on all of its aspects;

1.2. evaluate the results and draw conclusions as regards to their application;

1.3. be responsible for the exchange of information referred to the first subparagraph of Article 5;

1.4. keep abreast of national research being done in the fields covered by the concerted project and more especially of scientific and technical developments likely to affect the execution of the project;

1.5. suggest guidelines to the project leader.

2. The Committee's reports and opinions shall be forwarded to the Commission and to the Member States participating in the Project. The Commission shall forward these opinions to the CREST.

3. The Committee shall be composed of persons responsible for co-ordinating the national contributions to the programme and the project leader. Each member may be accompanied by experts."

"Article 5" states

"In accordance with the procedure to be adopted by the Commission in agreement with the Commitee (COMAC), the Member State participating in the project shall exchange regularly all useful information concerning the execution of the research covered by the project and forward to the Commission all information that may be useful for co-ordination purposes. They shall also endeavour to provide the Commission with information on similar research planned or carried out by bodies for which they are not responsible. This information shall be treated as confidential if so requested by the Member State which provides it.

"The Commission shall prepare yearly progress reports on the basis of the information supplied, and shall forward them to the Member States and to the European Parliament.

"At the end of the co-ordination period, the Commission shall, in agreement with the Committee, forward to the Member States and to the European Parliament a general report on the execution and results of the co-ordination action. The Commission shall publish this report six months after it has been forwarded to the Member States, unless a Member State objects..." (In this case a more limited circulation, if necessary in confidence, is authorized). (Official Journal of E.C. 1978).

The structure of the control of the project through a Concerted Action Committee on the Registration of Congenital Abnormalities which reported through the Commission to CREST left no rôle for either the Special Working Group EPID nor of the senior committee CRM in the supervision of the project.

In practical terms the Concerted Action Committee (COMAC) was of a varied composition (Appendix II) and it turned out in some countries that the persons placed on this committee did not have the time nor the influence to devote their attention either to carry out the duties or to disseminate or provide of information or to ensure adequate financing for the registers in the participating parts of their countries.

It should be said however that the activities of COMAC members in some of the Member States was diligent and effective, although the inevitable delays in reaching local agreements and ensuring adequate finance resulted in delays to establishing effective local participation.

The COMAC met seven times and the reports of their meetings were forwarded to the Commission. Secretarial duties were undertaken by the Project Leader and the supporting staff. The final meeting took place on February 16th 1982 and the final report took the form of two documents : a short Executive Report of activities, and a fuller report which included the working papers of the development phase from 1978 to 1981.

Following the approval of the European Commission on February 13th 1978 of the Concerted Action, the steps were taken to establish the "COMAC" for the study, and at its first meeting it approved the appointment of Dr. Josephine A.C. Weatherall as Project Leader to start work from 1st June 1978. In fact, the appointment had already been anticipated, and the Project Leader had already, in consultation with the members of SWG EPID, who were responsible for designing the project, decided that the Department of Epidemiology in the School of Public Health beside the Campus of the Medical School of the Catholic University of Louvain in Brussels, would make a convenient point for a Central Office. Although the Project Leader was domiciled in England it was found that the supervisory work of coordination was successfully maintained by about two visits totalling about 8 days each month.

One of the first problems was to choose a short title for the project. The acronym EUROCAT was chosen from the full title of the Study European Registration of Congenital Abnormalities and Twins.

One of the main difficulties at the start of the study, which continued unabated throughout, was the delay due to slow drafting in the E.E.C. of official contracts and of subsequent financial payments. For the first six months of the study the travelling expenses of the Project Leader and the assistant were paid from personal overdrafts. Although the contract, when signed, provided for the immediate payment of 10 % of the total sum, which was eventually justified at the end of the contract period, the sum provided usually covered only the repayment of the overdraft incurred in the waiting period. Similar delays were experienced throughout the study when a quarterly statement of expenses was presented to the Commission for reimbursement. The average delay was 2.9 months, with a range of between one and five months. Such delays in drawing of contracts and providing finance engendered considerable anxiety in the co-ordination team who were for months employed by the University of Louvain on a monthly basis by concession. No legal contract could be made in the absence of assured finances and any expenditure of moneys rested totally on the responsibility and private funds of the Project Leader. Starting the study in these circumstances was a hazardous undertaking.

2.3. The EUROCAT Study - objectives

The long term objective of the EUROCAT project is to test the feasibility of carrying out epidemiological surveillance in the countries of the EEC taking congenital abnormalities as an example. But an underlying and essential objective in the project has been to encourage European cooperation at all levels of workers in medical research.

The specific objectives are :

1) to establish in each country of the EEC one or more regional registers of congenital abnormalities providing reliable epidemiological information on the occurrence of the registered conditions in the progeny of the population living in the defined geographic area ;
2) to harmonise the methods of diagnosis nomenclature and of data collection in order to ensure the comparability of statistics between participating centres ;

3) to monitor the occurrence rate of congenital abnromalities in the progeny of different population groups in order to identify any unexepected frequency ;
4) to investigate the risk associated with possible teratogenic factors ;
5) to create in each country an area where reporting is reliable, so that base line rates are available for calibrating any information system established at national level for the detection of adverse environmental inlfuences ;
6) to evaluate the effectiveness and efficiency of screening programs, of preventive measures and of treatment methods ;
7) to provide a well documented set of cases recorded in a defined population for clinical research.

It was envisaged that these objectives would be best achieved if data about individual cases was accumulated at a central registry so that statistical analysis and monitoring could be carried out by controlled techniques and so that data was readily available from all registries to enable analyses to be carried out expeditiously.

2.4. The registers and their different development in 1978.

The official document announcing the study stated that the following Regional Registers would be included :

Belgium	Bruges* and Hainaut
Denmark	Odense
France	Paris*
Fed. Rep. Germany	Hessen
Ireland	Dublin and Galway
Italy	Florence and Rome
Luxembourg	Luxembourg
Netherlands	Leidschendam
United Kingdom	Belfast*, Glasgow* and Liverpool*

The first activity of the Project Leader after June 1st 1978 was to visit each of the named centres. This was accomplished during the first year, and the following notes describe, in brief, the findings at these visits.

All of these areas were visited by the Project Leader sometimes with the Assistant Project Leader.It became quickly evident that the delay between the visits made by the team involved in the feasibility study and the official approved of the study, the lack of any official news of the negotiations proceeding in the committees of the commission and the consequent uncertainty, left most of the areas without any financial provisions to make the necessary adjustments to adopt the actions implicit in the Concerted Action Project. As a result, only five of the Registers named in the initiating document, and shown by an asterisk in the list above, were in a position to start work in 1978. Four other registers were quite quickly planned so that 9 registers were able to commence reporting at the start of 1979, with two more starting during that year. In some countries reporting did not start until 1980 or even 1981.

Belgium - Bruges

A medical birth certificate had been used in West Flanders since 1965 covering approximately 14,000 births each year and this formed the basis of a system for notifying congenital anomalies to the local health officer. A health nurse gathered extra information from the local hospitals. This system however was producing, at that time, a very low apparent prevalence of malformations at birth. The medical birth certificate, piloted in West Flanders, was planned to be extended to the whole country from the start of 1979 and this data, when processed would provide denominators for both EUROCAT registries in Belgium.

Hainaut

No system for registering congenitally abnormal infant existed in the region in 1978, although a preliminary study carried out by Lechat and Borlée in 1972 had convinced the Belgian experts of the need for registers (vide supra) (Borlée et al 1977). The system to be developed in 1978 followed the methods used in the earlier trial which was based on cooperation between the main maternity hospitals and had been coordinated

by a doctor and a recording nurse. Planning for the establishment of a system, starting from January 1979, was well advanced and evident very good cooperation between paediatricians, obstetricians and pathologists had already been established in 1978.

Denmark - Odense

The visit to Denmark was delayed owing to exceptionally bad weather in the winter of 1978-1979, however when a visit was made in May of 1979 it became apparent that the local climate of opinion together with the excellent system of record keeping and good co-operation with the local public health administration made the setting up of a register a relatively easy process. However as had been stressed during the feasibility study the provision of funds for such an activity, which involved only the salary for a part time medical officer and a part-time clerk, was tenuous.

France - Paris

A system for medical notification of birth had already been exploited to notify babies with congenital malformations in three departments in the region of Paris since 1975 and the data had been processed and analysed by Institut National de la Santé et de la Recherche Médicale (I.N.S.E.R.M.) Although it was evident that information was relatively easily obtained in the Paris area, it was evident that many Parisienne mothers have their babies outside Paris and a substantial number of other mothers come to Paris from the provinces. It had therefore been decided to initiate a second study covering the resident population of the department of Yvelines, based primarily on cooperation between the medico-social system for care of the mother and child and on the maternity hospitals. This study was in course of development.

Morlaix

This registry which had existed since 1973 was added after the official start of the study in January 1978. A visit in October 1978 showed that the registry would be based on a local hospital and would cover, at best, only part of the department of Finistere. It was quickly apparent that about 25% of the more complex problems in obstetrics were refered either to Brest or to Paris. This applied particularly to antenatal diagnosis

and to termination of pregnancy, and there was no convenient way to find out about the normality of a fetus or child delivered outside the local area.

Federal Republic of Germany - Hesse

Although a system for notification of malformed infants at birth was established by law in the State of Hesse, as in other German States, there was substantial evidence to suggest that many of the babies with anomalies were not notified. As there was no means of identifying the children notified nor of linking records of malformations with records of live born infants nor with records of those which died, it was not possible to study the under notification in the region nor to establish locally a register of identified children.

Local attempts to define a smaller area of the State of Hesse from which a hospital based study of a resident population could be established, as in Hainaut in South Belgium, were frustrated by lack of financial support from either the State or the Federal Government at that time.

Luxembourg - Luxembourg

There was no existing system of notification of malformed infants nor any medical birth declaration on which such a notification system could be based. The first task in the country was seen to be the establishing of a system for medical registration of birth.

Ireland - Dublin and Galway

There existed already in Ireland two overlapping systems for collecting data on birth defects. One was concerned with the relation between birth defects and drugs used in pregnancy. Data was collected directly from labour rooms or from hospital notes in hospitals in many parts of Ireland. The second long standing system depended on a voluntary notification between hospital and community doctors and the research workers in the region of Dublin. Neither system appeared to be complete and there was no wish that either of these two systems should collaborate to form a single efficient register which would fulfil both existing functions in addition those of EUROCAT. There was therefore no suitable nucleus of a register existing at that time in either Dublin or in Galway.

Italy - Rome and Florence

In neither of the two areas put forward in Italy was any local registration of congenitally abnormal children being carried out in a comprehensive way. Some paediatricians in some of the hospitals were already cooperating with the scheme for the surveillance of malformations discovered at birth, the Indagine Policentrica Italiana sulle Malformazione Congenite (I.P.M.C.)organised by the National Research Council (CNR) of Italy centred at the Department of Pediatrics in the Catholic University of Rome. In neither of the areas concerned with EUROCAT were all hospitals covered by the I.P.M.C.

In Rome plans were being made with the regions near Rome to establish a regional register on the basis of cooperation with all maternity hospitals, but local agreement had not yet been achieved.

In Florence no registration system for malformations existed in the region of Tuscany although a system of health information to cover the whole region was envisaged and plans were well advanced to obtain population coverage for the Province of Firenze. This study would be based on about nine public and six private hospitals. As the study was being designed through the health department for the region the recruiting of the different specialist units, essential for obtaining good coverage, was well planned. But the actual development of a good working arrangement with the clinical doctors would be slow.

Netherlands - Leidschendam

This is the address of the Dutch Ministry of Health, and at the beginning of 1978 the EUROCAT register was still only a concept in the minds of doctors at the Ministry and was in very early stages of planning. No planning at a local level had yet been initiated nor any specific area designated.

United Kingdom

Greater Glasgow

The geographic outline of this area was satisfactorily defined but in starting the work considerable problems had been encountered in finding the malformed children and ensuring that the data about each child was complete. No single document existed with all the necessary data, and problems of obtaining records from different sources and of linking them were demanding an excessive load of inefficient clinical and clerical labour. There was, however, an enthusiastic and active local Registry Leader. Funds for the Register were provided entirely from the Greater Glasgow health budget and at the time there was no assistance from the research councils nor from the Scottish Home and Health Department.

Liverpool

This register had been in existence since 1961 and since 1975 had been financed by the Department of Health and Social Security. The area covered by the study was about to be extended to cover most of the connurbation of Liverpool. Local interest in the paediatric aspects of the register appeared active but there was apparently little cooperation with the obstetricians in the area and a total absence of local interest from pathologists.

Northern Ireland

In 1978 there already existed in Northern Ireland a system for bringing together all the public health records for children. Information from a medical notification of birth, was the starting point for a coordinated system of child health surveillance operated through the health visitors who work with and between the general practitioner doctors and the community physicians responsible for local child health.

The register was already funtioning moderately well and some research projects were underway. No special research funds for work with EUROCAT had been granted and the inevitable costs for running the register were entirely absorbed by the local health care nurses and doctors and by independently funded researchers in the University department of Medical Genetics.

Greece

The impending entry of Greece into the European Economic Community led to the proposal in November 1978 of a registry for Greece, and a visit was made to Athens in January 1979. At this time several ideas had been put forward for a study, none of which were compatible with gathering information for a defined resident population of women and their births. It was recognised that a new area of study should be chosen and the island of Evia was suggested as suitable.

2.5. Guidelines

In the period of development between 1979 and 1981, the operation of coordinating EUROCAT consisted mostly of patiently encouraging and advising many of the Registry Leaders in their efforts to establish an on-going local registration system. The central office devoted its attention to preparing for the reception, processing and storing of data and for analysing and preparing reports. At first guide-lines for procedures recommended for adoption at local level were prepared. The first guide lines concerned the registration of malformations and embodied all the agreements reached at the preliminary conference of Registry Leaders in January 1978. Only an outline is included herewith, since a revised version is printed in the EUROCAT Guide for the registration of Congenital Anomalies 1984. Revisions to the wording and methods are of minor detail and the methods established in the earliest stages of EUROCAT in 1978 and 1979 are still prevailing in the on-going study.

The general points covered in the guide lines were as follows :

Named records should be recorded at local level in order to link reports arriving from several sources and to avoid multiple registration; to facilitate the follow-up which may be required to confirm the diagnosis or to study the development of treatment and to trace children in order to conduct prospective or retrospective studies of treated children.

The Local Register should send to EUROCAT only the local number for each case, a limited list of data about the case, about the mother, the father and the diagnosis of all malformations.

Cases recorded at local level should include babies with single or multiple malformations. Attempts to establish discussions to define what is meant by a congenital abnormality or a malformation were circumvented by instructing the Registry Leaders to accept any baby reported with a condition which is mentioned in Chapter 14 of the International Classification of Diseases, 9th Edition (ICD 9), Volume I or to conditions included in its Index (Volume II). Conditions named "congenital", "inherited" or "inborn error" and mentioned in other Chapters should be sent to EUROCAT. However many minor and isolated malformations which are considered unimportant on their own are listed but not sent to EUROCAT. (See EUROCAT Guidelines series 1).

In cases where a diagnosis is in doubt, the case is recorded locally but is not notified to EUROCAT until the diagnosis is confirmed. New information received about a case after it has been notified to EUROCAT is included in an update report.

Names and addresses of cases and hospitals are NOT sent to EUROCAT. A local identity number, unique for each baby is sent to EUROCAT and is used in correspondence with the local register when there is need for extra information or further investigation. A standard pre-coded transmission form is used to transmit information from the Local Register to EUROCAT.

Provision for transmission of pre-coded case reports on magnetic tape with no supporting case documents have been made with some of the centres. This has presented some difficulties since only the coded items of data are provided. Data which is uncoded, such as drugs used or illnesses in the mother, which can be refered to quickly on the documents is not available in the EUROCAT centre for those registers.

There is no limit to the age of a child at which an anomaly may be detected or recognised, but at the start of registration and transmission of cases to the central registry it was agreed to concentrate on recording anomalies at birth. (As the study proceeded during the first four years, the need for extended observation both backwards into the gestation period to find the terminated pregnancies and forwards into the first year of life was recognised and reporting up to one year of age was practised by many of the registers by 1981).

Data processing

The development of the central system for processing the case reports from the registries, of the checking the data, the storage on magnetic media, and the preparation of tables from the stored data proceeded step-wise during 1979 and 1980. The first tables for circulation became available in March 1981.

Counting of babies

Many decisions were made in preparing the tables; particularly about how babies reported with more than one malformation should be considered. It was decided that in considering a single malformation, babies with one or more additional and different malformations would be counted along with babies having only that single malformation. It is therefore possible for a baby with five malformations to be counted five times; once for each malformation. It was essential therefore to make sure that the published tables are adequately annotated to show that the numbers of babies from two or more different malformation groups will give a count in excess of the total babies involved.
Sometimes a baby is reported with several malformations which all are included in one of the classes of malformations tabulated. For example a child without hands and toes will fall into the single class of limb defects. This baby will get counted only once although it had two distinct defects. WITHIN ANY CLASS OF TABULATED MALFORMATIONS EACH BABY IS COUNTED ONLY ONCE.

Recording of Multiple Births

As an additional objective of the EUROCAT study was to record all multiple births occurring in the offspring of women living in a defined geographic area. The recording of multiple births in the population, and basic information for transmission about zygosity was requested.

2.6. Confidentiality, Data Security and the Privacy of the Individual.

When the EUROCAT project was discussed with the Registry Leaders at the start of 1978, it was agreed that each Local Registry would record the identity of each malformed baby and of its parents along with a list of social and medical information about them. The use of named records at local level is essential a) to ensure that reports arriving from several sources can be associated with each other and so avoid duplicated registration; b) to allow follow-up which is sometimes necessary to verify or to amplify the diagnosis; c) to study the outcome of specific malformations, or to carry out prospective or retrospective enquiries.

Keeping such a register at local level raises the problem of privacy and confidentiality and of acceptability for the protection of families concerned and for the general population. It is thus essential that local conventional practices, as well as national regulations, are respected in each Local Register. The Registry Leader, or the Head of the Academic Department in which the Register is located, should have the necessary authority to enable him to be responsible for all aspects of the security of information within the Local Register and there should be clearly defined local rules governing the discipline of staff, the storage and security of documents as well as access to and use of the stored records on magnetic media and any data abstracted from them.

When the EUROCAT Central Registry was established in 1979 the responsibility for security of data sent to the EUROCAT Central Register rested jointly with Professor M.F. Lechat, Director of the Department of Epidemiology and the Project Leader of EUROCAT, Dr. J.A.C. Weatherall.

Because data is transmitted across international borders, strict precautions have been applied to ensure no unauthorised use is made of the data stored on magnetic media or on documents in the department or on the computer of Université Catholique de Louvain. The EUROCAT procedures adopted between 1978 and 1981 were considered to conform to the general principles recommended by the Assembly of the European Science Foundation in a 1980 statement concerning the protection of privacy and the use of personal data for research (ESF 1980).

The current procedures and precautions adopted by EUROCAT are outlined in the "Eurocat guide for the registration of congenital abnormalities" in EUROCAT GUIDE N°1 available from the central register in Brussels.

2.7. The Progress of EUROCAT

At the start of the study in 1978 none of the Registers were ready to start transmitting data to a central registry. During the period of waiting the Project Leader and part time assistant visited the Registers, drew up procedural guidelines and made preparations to automate the storage of data when it began to arrive. It was not until 1980 that the need for more clerical assistance at the Central Registry was felt and a data controller was engaged and trained.

The second priority was to investigate and find the ways of eliminating differences in diagnosis of the conditions reported. Differences appeared to exist in the diagnosis of zygosity in multiple births, in the nomenclature of different types of malformation of the Central Nervous System ; in procedures followed by those practising fetal and perinatal pathology ; in the description and the nomenclature of cardiovascular defects ; and in the description and classification of limb defects. The period when the Central Registry was waiting for data from the local registries was occupied in holding workshops on some of these topics.

2.7.1. Workshop on the determination of zygosity at multiple births.

The first of the consultations concerned the recording of zygosity in multiple births.

Although multiple births occur between 1.25 to 2.50 per cent of all births, the accurate recording of data available at birth is usually neglected and the subsequent decision about zygosity, for the like sex pairs, is usually estimated on a basis of physical likenesses and confirmed, where necessary, by matching of blood groups and tissue types.
In the absence of reliable data recorded at birth the survival patterns of monozygous and dizygous sets is not usually estimable since after one twin has died there is usually no means of confirming zygosity.

In an attempt to improve the observations on multiple births made routinely at birth, a workshop was organised at which the methods advised by Professor Derom of University of Gent and Drs. Vlietinck and Van den Berghe of University of Leuven were discussed by a group of Registry Leaders and their deputies. These methods appeared to be straightforward and did not seem unduly costly, and the authors were therefore asked to prepare short texts of guidance for obstetricians, pathologists and labour room staff with a view to improving the routine recording at multiple births. These texts are printed and available from the Central registry.*

2.7.2. Workshop on Congenital Malformations of the Central Nervous System

The second field of doubt which concerned EUROCAT was in the description and nomenclature and classification of the gross abnormalities of the Central Nervous System. These appeared to be two separate problems. One concerned the recognition of and name given to the anomaly and the second concerned the grouping of anomalies for statistical purposes.

* EUROCAT guide to the diagnosis of zygosity at multiple births by R. Derom. EUROCAT guide to the confirmation of zygosity diagnosis of multiple births by Robert F. Vlietinck and Herman Van den Berghe available from EUROCAT central registry, U.C.L.-EPID.30.34, Clos Chapelle-aux-Champs, 30, 1200 Brussels.

A group of consultant experts from embryology, from developmental anatomy, from pediatric neurology, from pediatric surgery were invited to assist Eurocat on these problems.*

Many of the fetuses born with gross Central Nervous System defects are dead at birth and therefore become recorded among the still births. In many countries there is no legal obligation to record or certify the cause of still birth. In some countries, the certification of still birth and the diagnosis is recorded by the birth attendant who may be a midwife. The group agreed that some guidance for distinguishing the main types of gross anomalies would be of use to midwives and nurses and would assist in arousing their attention towards the importance of consulting paediatricians or pathologists and of encouraging parents to request a detailed examination of every child born dead or dying in infancy. It was agreed that Professor Nevin and Dr. Weatherall would prepare a book of typical photographs contributed or selected by members of the group, and a text of descriptive definitions was agreed. This book was published in 1983 (Nevin and Weatherall 1983).

In order to ensure that the statistical classification of anomalies of the Central Nervous System was improved from that included in the present 9th Edition of the International Classification of Disease, the experts reviewed the terms included in the existing classification and offered a revision which is reprinted in appendix III.

* Consultants at Central Nervous System Workshop : Professor Verne S. Caviness, U.S.A.; Professor P. Evrard, Belgium; Dr. Angus Gibson, United Kingdom; Professor F. Gullota, Federal Republic of Germany; Mr. L.P. Lassman, United Kingdom; Professor K.M. Laurence, United Kingdom; Professor G. Lyon, Belgium; Dr. Pierpaolo Mastroiacovo, Italy; Professor N.C. Nevin, United Kingdom; Professor Charles Roux, France.
Workshop organisers : Dr. J.A.C. Weatherall, Project Leader EUROCAT; Dr. Philippe De Wals, Assistant to Project Leader.

2.7.3. Workshop in Fetal and Paediatric Pathology.

One of the principle difficulties encountered during the preliminary consultations between the Project Leader and the Registry Leaders concerned the difficulty in obtaining post mortem examination of still born and perinatal deaths and particularly in ensuring the examination of material from spontaneous abortions and terminated pregnancies. Pathological investigations and dissections were not carried out in many of the register areas, ostensibly because "the parents would not want it". However it became rapidly apparent that in the very few centres where a paediatric pathologist was working with obstetricians and paediatricians, the post mortem rate was high. It was therefore decided to try to promote the training and establishment of paediatric pathologists in the registers, first by holding a workshop to which many pathologists known to be practising fetal and perinatal pathology in Europe were invited.*

The group recognised the following important points. In recent years there has been an increasing demand from parents for information about the factors leading to the birth of a malformed child or of a child with a biochemical anomaly. Many parents no longer accept such a child as an "Act of God", and want to be assured that any further children born will not be similarly affected. The same assurance is

* Consultant pathologists at the Workshop in Fetal and Perinatal Pathology in Sheffield. June 10-12 1980 : Dr. L. Ayres, Portugal; Prof. F. Beck, United Kingdom; Prof. C.L. Berry, United Kingdom; Dr. N.J. Brandt, Denmark; Dr. J.N. Cox, Switzerland; Dr. J.D. Elema, Netherlands; Dr. A. Giannini, Italy; Dr. A. Gibson, United Kingdom; Dr. Y. Gillerot, Belgium; Prof. M. Hauge, Denmark; Dr. E. Kaslaris, Greece; Dr. P. Kelehan, Ireland; Dr. R. Laurini, Norway; Prof. T. Pexieder, Switzerland; Dr. J. Rapola, Finland; Dr. H. Rehder, German Federal Republic; Dr. C. Roux, France, Dr. S. Salvadori, Italy; Dr. A. Skordalakis, Greece; Mrs. A. Smith, United Kingdom; Prof. R.W. Smithells, United Kingdom; Dr. I. Tygstrup, Denmark; Prof. Dr. M. Vogel, Federal Republic of Germany.
Workshop Organisers : Dr. J.A.C. Weatherall, Project Leader EUROCAT; Prof. J.L. Emery, Sheffield, United Kingdom.

sometimes needed for parents who, themselves have had a treated or untreated malformation or anomaly. Many women are now accepting offers, and others demanding the provision, of pre-natal diagnosis through ultra-sound examinations, alfa-feto-protein screening (AFP) and amniocentesis so that they may avoid giving birth to an affected child. This service, in turn, leads to therapeutic abortion of affected fetuses. All this material should be examined, if only to ensure the correctness of the diagnosis.

At the same time, persons concerned about potential dangers to their progeny from environmental pollution or from substances encountered at work, wish to be reassured that dangers do not exist or that such dangers will be quickly recognised.

In order to establish the presence or absence of such dangers, and to monitor the effectiveness of intervention procedures such as pre-natal diagnosis, it is desirable to measure the abnormalities occurring in the children born, and in the fetuses which are shed spontaneously or deliberately during pregnancy. The spontaneous loss of an increasing number of abnormal fetuses or of a change in the pattern of abnormalities seen, may be the first sign of the influence of an environmental toxic substance. The examination of the early aborted fetus is likely to become a powerful way of detecting such influences, as has been suggested by Kline, et al (1977).

Examination of shed fetuses at all stages of gestation is being requested more and more. It demands skill which is not usually available in a department of general pathologists working in rotation who are coping with the routine demands for necropsy and biopsy examinations arising from investigations of the adult population. Moreover, as medical science advances, the loss of infants at, or shortly after, birth is becoming more often explained by anomalous biochemical or anatomical development and more extensive examination of dead children is requested.

The monitoring of malformations found at birth in living children, or in those which die, will not suffice to answer the questions

about rising or falling incidence unless there is good information about the pregnancies which are terminated because an anomaly is suspected or about those which terminate spontaneously.

The work needed in the field was seen to fall in several parts according to the development of the fetus : the pre embryonic stage; the embryon stage up to 30 mm length : the larger fetus (over 30 mm) and the perinatal necropsy of still or live born infants.

Recommendations for procedures of examining and recording data about material and the equipment required for examining each of these different groups is available in a hand book from the EUROCAT central office.*

The consultants particularly stressed the consideration of professional work load in fetal and paediatric pathology. The time to carry out an examination was inversely proportional to the size of the material examined.

In general, it was agreed that a pathologist can handle no more than 180 necropsies a year, and that the total time taken by a doctor for the full (naked eye, histology etc.) examination of one child was about 10 hours. To achieve this output, it was reckoned that one pathologist requires a back-up of two full-time technicians, in addition to the usual secretarial and filing services.

In addition, it should be realised that the development of an adequate fetal and perinatal pathology service will inevitably increase the use of hospital photographic and x-ray departments as well as microbiology and biochemistry services.

* EUROCAT guide to a service in fetal and perinatal pathology - estabishing a service, by J.L. Emery and J.A.C. Weatherall, available from EUROCAT central registry, U.C.L. - EPID 30.34, Clos Chapelle-aux-Champs, 30, 1200 Bruxelles.

Training and Use of Personnel.

There is, at present, an inadequate number of trained persons to carry out work in fetal and perinatal pathology in all parts of Europe.

In some centres it may be possible to recruit the services of human embryologists in University Departments of Anatomy, who after special training can make major contributions in the examination of special tissue and organ studies. In addition non-medical biological graduates may be trained to carry out much of the preliminary screening of the sections and material, as is already carried out in the field of cytogenetics and in cancer screening cytology.

2.7.4. Workshop on Down Syndrome

Down Syndrome (D.S.) is a major cause of mental defect in most western populations, and its prevention is of major importance in public health. The risk of bearing a D.S. child increases with maternal age so that the rate doubles with each five year increase in age after 30 years. It is possible to diagnose the condition by sampling fetal tissues in utero by carrying out amniocenteesis. The risk of this procedure in precipitating an early end of the pregnancy is not negligible, but the incidence of the Down Syndrome in older women, and therefore the chance of finding cases, is sufficiently high to justify the considerable risks and financial costs of the investigation. Many countries in which legal termination of pregnancy is permitted now offer antenatal diagnosis to the older mothers. It should not be overlooked that this method of prevention by intervention will not affect the D.S. children born to younger mothers which in many countries accounts for over 70% of the D.S. children born.

The risks of loosing a pregnancy following amniocentesis and the huge work load involved in carrying out antenatal diagnosis as a screening procedure for infants of mothers of all ages make this method of prevention undesirable. Therefore it is of major

importance to attempt to establish reliable risk factors for the younger women so that such women may be offered antenatal diagnosis and further reductions in the D.S. children born can be acheived. In order to review possible lines of investigation a workshop of experts was held in Brussels on July 13th-14th 1981.*

There was wide ranging discussion about research techniques under development and their application to research in Down Syndrome, and two studies were suggested at this workshop. One would involve detecting the slow growth of the Down Syndrome fetus during early pregnancy in young women by the use of serial ultra sound measurements. This would provide a non-invasive method of detecting abnormal fetuses.**

It was generally agreed that too little is at present known about the D.S. families. A second study would aim to identify the factors associated with the occurrence of non-disjunction by identifying the donor parent for each Down Syndrome child and the time at which the faulty chromosomal division has occurred. Recent work with karyotype analysis has allowed the identification of the parent who has contributed the trisomic chromosome. The separation of data about D.S. families according to both the donor parent and the time at which the aberrant meiotic division has occurred should allow differences, if any, to be more clearly exposed. Attention should be focussed on the younger mothers and the following questions answered :

* Participants at Down Syndrome Workshop - Brussels July 13-14 1981 : Dr. M. Mikkelsen, Denmark; Dr. Lucien Koulisher, Belgium; Prof. Norman C. Nevin, United Kingdom; Dr. Philippe De Wals, Belgium; Dr. Malcolm A. Ferguson-Smith, United Kingdom; Dr. Anders Green, Denmark; Dr. Pierpaolo Mastroiacovo, Italy; Dr. J.A.C. Weatherall, EUROCAT Project Leader).

** Recent work by WALD, et al. 1984 suggests that abnormally low AFP at 16 weeks gestation can be used as a reliable indicator of slow fetal growth. Ed.

a) which parent has contributed the trisomic chromosome ?
b) at which period did the non-disjunction take place in the parent ?
c) are there any differences in the background features of the parents of the different causal groups ?
d) can any regional differences be seen in the data ?
e) are any racial differences apparent ?

Both these studies are being developed as independent satellite or parallel studies within the framework of the Medical Research Program. The first as part of the work of the fetal monitoring group and the second as the non-disjunction study.

2.8. Further activities in coordination of EUROCAT.

2.8.1. Registry Leaders Conferences

A second and third conference for Registry Leaders was held in January 1980 and November of 1981 respectively. The Second Registry Leaders' Meeting reviewed and amended some of the decisions made at the first 1978 conference. The third meeting reviewed the first results of the study and the progress made in the four pilot years. By this time most leaders were convinced of the need to extend case finding up to 1 year of age and on into childhood as soon as the means could be found. In addition the meeting included some scientific studies made within the local registers and presented by local Eurocat staff or by collaborators.*

* "Working papers of the E.E.C. Concerted Action Project EUROCAT available from the EUROCAT central office in Brussels.

2.8.2. Exchange of personnel

A further step in coordinating EUROCAT has been through the promotion of meetings between persons working with Eurocat registers. An essential part of the Eurocat project has been to facilitate international cooperation between registry staff of all levels.

A meeting of statisticians held in spring 1980, was attended by 12 persons responsible for the handling of local data. At this meeting the main problem discussed was the obtaining of statistics concerning the total births occurring to women in the surveyed area and among which the babies with congenital anomalies are discovered.

Registry Workers exchanges. In order to begin to introduce the different registry workers to each other, a series of tours have been organised. The First Registry Workers tour took place in October 1980. Eight workers from Odense, Paris, Luxemburg, Hainaut, Flanders and Firenze Registers visited Liverpool, Dublin and Belfast in a 5-day tour. A Second Registry Workers tour included workers from Rome, Firenze, Ferrara, Dublin, Liverpool and Belfast who visited Paris and Brussels. Unfortunately, a planned visit to Denmark on this tour had to be cancelled because of travel difficulties, but two of the team from Odense were able to travel to Brussels to describe and discuss their methods with the group of Registry workers. During these tours members discussed with each other about difficulties in case finding, in coding and in maintaining accurate up to date registration. Representatives from Eurocat central registry accompanied the tours and gave some tuition during the courses.

During the preliminary visits to the registries made by the central coordinating staff, the lack of a service in perinatal pathology was apparent in many of the centres. In order to stimulate the development of the speciality EUROCAT has financed the attendance of young pathologists to the four annual Advanced Training Courses in Paediatric Pathology held at centres in Europe between 1979 and 1982.

2.9. The Registries and their data at the end of the development phase.

By the end of 1981, a total of eighteen registers were actively reporting to the EUROCAT centre in Brussels covering about 197,000 births each year. Centres in two countries outside of the community, in Switzerland and Yugoslavia were planning to join the study. A list of registers and their leaders is shown in appendix IV.

The performance of each the Register was reviewed critically by P. De Wals in 1981 and an estimate of coverage for case finding among the surveyed births in the study area was made where possible. The full text of Dr. De Wals' report is printed in the "Working papers of the E.E.C. Concerted Action Project EUROCAT" *.

Comparisons of the numbers of babies reported from each centre and on the types of malformations reported have been issued as EUROCAT REPORTS from 1980 onwards *. During the first phase of the Study there has been more concern with how well the registers are functioning. Are all the babies being found ? Is all the appropriate data being recorded ? It is only after these questions have been answered in the affirmative that the data from the different registers can be validly compared and perhaps pooled for further analysis. A fuller analysis of the data collected up to the end of 1982 is in preparation and will be published in the EUROCAT Series*.

2.10. Some early results and analysis of differences.

EUROCAT has been developed as a tool to monitor the occurrence of congenital abnormalities in the E.E.C. member states. In the first four years the different parts of the tool have started to contribute data and differences in incidence are apparent between the different countries.

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* Available from EUROCAT Central Registry - U.C.L.-EPID 30.34, Clos Chapelle-aux-Champs 30, 1200 Bruxelles.

Variations in incidence of congenital anomalies can be due to a number of factors. They may be due to environmental or genetic differences in the populations studied : to the methods used to diagnose, to trace and to record the cases : or they may be random. Are the differences due to artefacts of data collection or are they "real" ? Can EUROCAT yet be used as a reliable tool to indicate environment changes ?

The data accumulated in this development stage shows that there are fundamental differences in the time of case finding which makes it difficult to measure the prevalence at birth in some registers. The analysis which follows* has concentrated on the "annual cohort incidence". This is calculated by taking the number of abnormal babies, born in the year concerned, in which an abnormality has been reported at any time from birth onwards, and expressing this total as a fraction of the total births in that year times 10,000 : thus giving the "cohort incidence rate".

Table 2.10.I. shows the annual cohort incidence rates for all the abnormal babies born in registers from 1979 to 1981.

* This analysis was carried out by Dr. P.P. MASTROIACOVO and Dr. J.A.C. WEATHERALL and communicated to the Regional meeting of the International Epidemiology Association at Singapore, October 1983.

TABLE 2.10.I.

MALFORMED BABIES IN 1979, 1980 AND 1981
TOTAL INCIDENCE OF BABIES WITH CONGENITAL ABNORMALITIES RECORDED IN EACH BIRTH COHORT

		Proportion per 1,000 total births		
		1979	1980	1981
COUNTRY	REGISTRY			
Belgium	West Flanders	1.69	1.25	1.10
	Hainaut	2.09	2.46	2.75
Denmark	Odense	2.42	2.35	2.67
France	Morlaix	1.81	1.01	0.99
	Yvelines	1.61	1.07	-
	Paris	-	-	2.08
Germany	Berlin	-	1.62	4.58
Greece	Evia	-	-	1.53
Ireland	Dublin	3.53	2.83	3.10
	Galway	-	-	2.13
Italy	Firenze	2.29	2.27	2.04
	Umbria-Lazio- Roma	0.94	2.04	1.75
	Emilia-Romagna	-	1.86	1.56
Luxembourg	Luxembourg	-	1.42	1.54
The Netherlands	Groningen	-	-	1.97
United Kingdom	Belfast	2.55	2.19	2.11
	Glasgow	1.64	3.33	3.25
	Liverpool	3.18	2.10	1.97

In order to see whether the high rates of reporting from some centres was due to excessive recording of mild conditions or conditions where there may be doubt that an anomaly exists, anomalies were divided into two groups : "mild conditions" and "significant conditions". The mild conditions include - ear anomalies, male external genital anomalies, patent

ductus arteriosus, unspecified heart murmurs, congenital dislocation of the hip, talipes, minor limb anomalies (not reduction deformities), skin tags and other unspecified anomalies. All others malformations were regarded as significant conditions. Figure 2.10.a. compares the frequency of the two groups of conditions for each centre. It is clear that variation affects both groups of condition, and there is a significant correlation between their frequencies (r = 0.95 : z = 3).

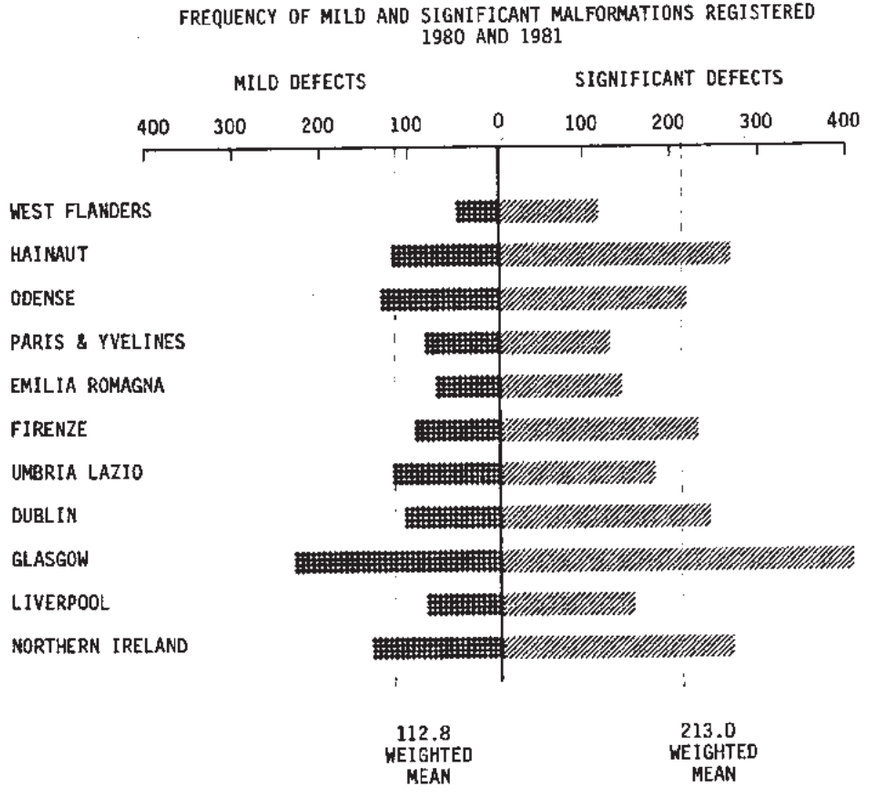

FIGURE 2.10.A.

Eleven of the EUROCAT registries are listed in Table 2.10.II. Each reported over 9000 births in the years 1980 and 1981 and reported cases regularly to EUROCAT.

TABLE 2.10.II.

TOTAL BIRTHS SURVEYED IN ELEVEN OF THE LARGER EUROCAT REGISTERS IN WHICH MORE THAN 9,000 BIRTHS HAD BEEN SURVEYED IN 1980 AND 1981.

		Total births 1980 and 1981
Belgium	West Flanders	12,936
	Hainaut	16,653
Denmark	Odense	9,750
France	Paris	39,000
Ireland	Dublin	51,601
Italy	Emilia-Romagna	26,793
	Firenze	18,932
	Umbria-Lazio	18,243
United Kingdom	Belfast	56,391
	Glasgow	26,929
	Liverpool	40,904
	TOTAL	318,132

Analysis of differences of the "significant" conditions

In order to examine further the differences between the eleven registers, eight specific groups of the "significant conditions" were analysed.

1) neural tube defects;
2) hydrocephalus;
3) specified cardiovascular abnormalities (VSD, ASD, common truncus, transposition of great vessels, tetralogy of Fallot, common ventricle, endocardial cushion defects);
4) facial clefts;
5) intestinal atresias;
6) renal and urinary tract anomalies;
7) limb reduction deformities;
8) Down syndrome;

Cohort incidence rates for the two years together are shown in table 2.10.III.

TABLE 2.10.III.

COHORT INCIDENCE RATES PER 10,000 TOTAL BIRTHS FOR SPECIFIC MALFORMATION GROUPS IN ELEVEN EUROCAT REGISTRIES IN 1981 AND 1982.

	Neural Tube defects	Hydro-cephaly	Specified cardiac defects	Facial clefts	Intestinal atresias	Renal and urinary anomalies	Limb reduction anomalies	Down Syndrome
West Flanders	7.7	4.6	7.7	10.8	9.3	5.4	7.0	8.5
Hainaut	9.6	4.8	64.2 ====	18.0	8.4	10.8	4.8	10.2
Odense	11.3	5.1	25.6	23.6	9.2	14.4	6.7	4.1
Paris	7.9	6.1	15.9	9.7	5.6	6.7	3.6	11.5
Dublin	42.4 ====	7.4	21.9	17.4	6.4	10.7	3.7	16.7
Emilia Romagna	6.3	4.1	13.8	9.3	4.5	5.2	5.6	14.6
Firenze	12.7	7.4	44.4	13.2	7.9	19.5 ====	6.3	19.0 ====
Umbria-Lazio	6.6	6.6	11.0	9.9	5.5	7.7	5.5	15.3
Belfast	40.2 ====	5.3	22.9	16.0	9.8	12.2	8.3	13.1
Glasgow	19.3	8.2	45.3 ====	17.8	10.4	19.3 ====	8.2	7.1
Liverpool	19.8	3.4	39.1	12.2	6.4	8.8	5.9	8.6

(Significantly high is marked === and low --- P > 0.05)

The table shows which rates are outstandingly high or low. The ratio of observed to expected numbers has been used with the expected number calculated from the "weighted mean" number or the mean of the mean numbers for each centre and each malformation group. It shows also some important points :

Neural tube defects are high in all parts of Ireland, lower in Glasgow and Liverpool where AFP Screening programs are in practice and notably lower in all other European centres.

Specific cardiac defects are notably high in Hainaut, Glasgow and Firenze. The explanation is not obvious but all are centres with very active cardiologists. Early diagnosis and case finding may be the cause.

Facial clefts is very high in Odense which is consistent with data reported by the ICBDMS* where all Scandinavian countries are reported with high rates.

Renal anomalies are high in Firenze and Glasgow. The reason is not obvious but may reflect a high level of involvement of paediatric pathologists in investigation of still births in these areas. These findings need further investigation.

Down Syndrome is outstandingly high in Firenze. However the comparability of rates calculated over all maternal ages is suspect. A large proportion of women having infants at older ages coupled with early diagnosis could explain the high rate observed. Proper analysis of D.S. would involve comparing the incidence in smaller groups at the different ages. Such analysis requires details of maternal age for the total births in each register for each year. Such details are only obtained after considerable delays and were not available at the time of the review discussed here.

For limb reduction anomalies, intestinal atresias and hydrocephaly there are no outstanding differences, all the rates being distributed within "normal limits" of the overall mean rates for all centres.

* See page 9.

The fact that in these three groups of clearly recognisable defects there are no outstanding differences between the registers helps to dispell the general notion that differences between registers are due to better or worse case finding. Evidently the variation observed for these groups of defects could have occurred by chance, and other differences observed are likely to be real. It is not helpful to assume that the presence of clinical specialists in an area accounts for the high rates. The speciality may have developed in that centre because of the high incidence rather than be the cause of complete case finding.

Further exploration of the differences and similarities between the EUROCAT registers is now proceeding and periodic publication of analyses with tables and commentary on the findings will be made in the EUROCAT Series.

3.0. COMMENT

The preliminary analyses of EUROCAT data collected during the pilot years 1979-1981 are reassuring in showing that the methods of data collection adopted have ensured reasonably complete data collection with adequate accuracy. Some long known regional differences have been confirmed and new differences have become apparent. It is evident too that the registers are able to maintain a consistent level of case finding.

Case finding can present considerable problems for registers. Those centres with automated centralised patient health care summaries are at an advantage. Here the scanning of the case load of all departments of all hospitals can be carried out regularly by means of acquiring selective lists of case numbers where a diagnosis of an anomaly has been recorded. Adequate arrangements for cross reference between hospital and register ensure that cases, not so far registered, can be located and arrangements made to view the case records. Such methods reveal that babies with anomalies may be found as patients attending almost any specialist branch of a hospital, especially as outpatients. Notable departments involved are orthopaedics, skin and plastic surgery as well, of course, as general paediatric physicians and surgeons, cardiologists, and pathologists. Finding new cases is a considerable load for those registers which are not able to obtain routine lists of records, and have to depend on willing cooperation and notification of cases from their many clinical colleagues.

Some problems faced in running a central register are inevitable. The delays in case finding and processing at local level are bound to affect the time lags encountered in receiving data at the central registry. Any editing enquiries made at the central office often require a two stage enquiry - to local register and thence to the hospital - before the question can be satisfactorily answered.

At local level the relationships of the people working in the register to their surrounding medical colleagues is crucial. Bad relationships can ensure poor case finding. The only action open to the staff of the Central Register is persistently to encourage the local registers to find

ways of serving the local medical community so that a core of local interest is developed and local clinicians see its uses and become protective towards the register.

The EUROCAT registers form a network which serves to establish basic and comparable standards in registration of congenital abnormalities in a way suitable for each individual country. The development of a register in any part of any country depends on the interest of the local clinical doctors and the problems present in the community and it is not by chance that registers developed in United Kingdom in Glasgow, Belfast and Liverpool where high incidence of central nervous system defects existed, and in other parts of Europe where the presence of a high incidence of malformations suggested a problem for those populations.

The cooperation of the registers allows surveillance to be carried out on a population of 200,000 births a year - a task which could be achieved with national data within some countries if all parts of those countries could be willing to cooperate to achieve good registration. The larger the areas studied within a country the more likely that some of the areas in the study will not cooperate efficiently.

A further potential which has not yet been realised is that researchers wishing to consider rare types of defects can be put in touch with clinicians in different parts of Europe from which similar types of condition have been reported.

The regular contacts maintained between the registers ensures a network of clinical consultants and experts who are willing to respond to any emergency enquiry should one arise.

The use of the EUROCAT registers for cooperative research projects is complex. Most local registers are staffed to achieve the job of registration. Any research involving extra finding of records or making contacts with clinicians is commonly not allowed for in the funding, and excessive costs become a barrier to action when EUROCAT central office initiates more than a routine enquiry. If the EUROCAT data is to be used effectively for research, especially for answering rapidly questions

about possible causation of epidemics, then funds must be available. Either these should exist at local level to be used for local research but potentially available with priority for use in dealing with EUROCAT queries, or the funding of the Central office should include provision for research officers who can travel round the centres to help to carry out the relevant enquiries. The first option seems more expedient in reducing funds spent on travelling and overcoming any language problems : however EUROCAT should however have funding to bring such researchers together to ensure that common methods are adopted. Probably a combination of both types of funding would be ideal.

The task of monitoring the cases provided by careful registration of abnormal children is impossible without adequate information about the births which form the "population at risk". Limitations of the intepretation of data on Down Syndrome are illustrated on page 43 and are due to lack of detailed analysis of the ages of the mothers at birth. Such data is usually collected and analysed for each EUROCAT area in each country. The location of the source of such information and the arranging for appropriate tabulations to be made involves considerable care and delay. These tasks must be viewed as an essential task of the EUROCAT project.

More than ever now is the need to study the reasons for the great differences seen between centres. Is the absence of malformations of the Central Nervous System on the European continent a reflexion of dietary habits ? Do the continental women eat more salads than their island neighbours in the British Isles ? Does the fetus of Italian or South Belgian parents respond to a poor maternal diet by a different failure of development than is seen in Ireland ? The further steps of individual studies of cases, and of diagnoses in cooperating EUROCAT registers will establish that like is compared with like and will help to set up the firm basis upon which causal factors during the pregnancy may become apparent.

The EUROCAT central registry is established. Data is available and the tasks set for the development phase of EUROCAT have been achieved. The intermittent contact between the Registers and the Central Office continues and a dialogue about diagnosis, about coding and about the results

of tabulations performed is all the time training the registry staff in knowledge of different types of anomaly and the problems in case finding and the Registry Leaders in the importance of rigorous methods in collection of data, a fundamental of reliable epidemiology. The tasks of the central office may change as the study proceeds from those of stimulating case finding at local level to those of carefully watching both increases and declines in the reporting and of initiating enquiries when needed. In February 1978 EUROCAT did not exist. By the end of 1981 an active enthusiastic group of specialist registers has been established.

Congenital malformations are rare, and even if all trivial conditions are included they affect scarcely more than 5% of children born. But to the parents of a seriously defective child malformations are of immense importance, and to the exchequer which provides the medical and social care, children with developmental defects and malformations account for a substantial proportion of the funds used for medical care of children in many diverse departments of a modern hospital.

The foundations for further studies are well laid in Eurocat : the next few years should see useful diagnostic and etiological studies in action.

4.0. REFERENCES

AREY, L.B.
Developmental Anatomy 7th edition (revised).
Saunders W.B. and Co. Philadelphia and London, 1974.

BARROW, M.W. and TAYLOR, W.J.
A rapid method for detecting malformations
in Rat Fetuses J. Morph., 1969, 127 : 291-306.

BENIRSCHKE K.
Accurate recording of twin placentation.
J. Obstet. Gynec. 1961, 18, 334.

BIRBECK, J.A.
Biology of Human Fetal Growth,
Edit. Roberts D.F. and Thomson A.M. : Taylor and Francis, London, 1976, 39-68.

BORLEE, I., LECHAT, M.F., BOUCKAERT, A. and COLTRO, A.
Une enquête régionale sur les malformations congénitales.
Louvain méd., 1977, 96 : 121-134.

EUROPEAN SCIENCE FOUNDATION (ESF) : Statement concerning the protection of privacy and the use of personal data for research.
Adopted November 1980, ESF, Strasbourg.

EUROCAT Guide for Registration of Congenital Anomalies.
November 1984. Available from EUROCAT EPID 30.34-U.C.L. 1200 BRUSSELS.

CASSER, R.F.
Atlas of Human Embryos, Harper and Row, Hagerstown, Maryland, New York, Evanston, San Francisco, London, 1975.

HAMILTON, W.J., BOYD, J.D. and MOSSMAN, H.J.
Human Embryology 4th edition.
Heffer, Cambridge : William and Wilkin, Baltimore, 1972.

ICBDMS - INTERNATIONAL CLEARINGHOUSE FOR BIRTH DEFECTS MONITORINC SYSTEMS. Annual Reports 1981 and 1982.
Stockolm, Garnisonstryckeriet. Circulated by ICBDMS, Sylvia HAY, 414, 20th Street, San Francisco Cal. 94114, USA, 1983.

Journal Official of the E.E.C.
L 52 of 23rd February 1978, 20-28.

KENNEDY, W.P.
Epidemiologic aspects of the problem of congenital malformations.
Birth Defects, Orig Art Ser III, 1967, n°2, 1-18.

KLINE, J., STEIN, Z., STROBINO, B., SUSSER, M. and WARBURTON, D.
Surveillance of Spontaneous Abortions : Power in environmental monitoring : Amer. J. Epidem., 1977, 106 : 345-350.

LECK, I.
Correlations of malformation frequency with environmental and genetic attributes in man
in Wilson, J.G. and Fraser, F.C. (eds.), Handbook of Teratology, Vol.3, Comparative, Maternal and Epidemiologic Aspects, New York, Plenum Pub. Co., 1977, 243-324.

MACGILLIVRAY I., NYLANDER P.P.S. and CORNEY G.
Human multiple Reproduction.
Saunders C°, London 1975.

MOURANT A.E., KOPEC A.C. and DOMANIEWSKA-SOBCZAK K.
The distribution of the human blood groups and other polymorphisms.
Oxford University Press, 1976.

MOTULSKY, A.G., LENZ, W. and EBLING, F.J.G., Editors.
Birth defects - proceedings of the fourth International Conference : Vienna, Austria 2-8 September, 1973.
Exerpta Medica, Amsterdam, 1974.

NEVIN, N.C. and WEATHERALL J.A.C.
Illustrated Guide to Malformations of the Central Nervous System at Birth.
E.E.C. - Churchill Livingstone, Edinburgh, 1983.

O'RAHILLY, R.
Early human development and the Chief sources of information on staged human embryos.
Europ. J. Obstet. Gynae. Reprod. Biol., 1979, 9/4 : 273-280.

STEVENSON, A.C., JOHNSTON, H.A., STEWART, M.I.P. and GOLDING, D.R.
Congenital Malformations.
World Health Organisation, Geneva, 1966.

STREETER, G.L.
Developmental Horizons in Human Embryos : age-group XI 13 to 20 somites and XII 21 to 29 somites.
Carnegie Contrib. Embryol., 1942, 30 : 211-245.

STREETER, G.L.
Developmental Horizons in Human Embryos : age-group XIII - XIV.
Carnegie Contrib. Embryol., 1945, 31-63.

STREETER, G.L.
Developmental Horizons in Human Embryos. Description of age groups XV and XVI, XVII and XVIII.
Carnegie Contrib. Embryol., 1948, 32 : 133-203.

STREETER, G.L.
Developmental Horizons in Human Embryos. Description of age-groups XIX, XX, XXI, XXII and XXIII.
Carnegie Contrib. Embryol., 1951, 34 : 165-196.

WILSON, J.G.
Methods for administering agents and detecting malformations in experimental animals
in "Teratology Principles and Techniques". (Wilson, J.G. and Wakely, J. eds.) Univ. of Chicago Press, Chicago, Illinois, 1965 : 262-277.

WILSON, J.G.
Environment and birth defects.
Academic Press, New York, London, 1973.

W.H.O.
Working document CM/DSI/HSM/WP/72.4.
Consultants' report on WHO's proposal for a study on congenital malformations.
November 1970.

W.H.O.
Report DSI/72.7.
Consultation on WHO Program of congenital malformations reporting 24-28 July 1972, Geneva.

APPENDIX Ia.

Members of First Planning Workshop. November 18th - 19th 1974 Brussels.

Dr. R. BECKERS	Ministry of Health	Brussels	Belgium
Dr. Z.J.BRZEZINSKI	W.H.O. European Regional Office	Copenhagen	Denmark
Dr. J. CLEMMESEN	Finsen Institute	Copenhagen	Denmark
Dr. G. DEAN	Medico Social Research Board	Dublin	Ireland
Dr. K.H. DEGENHARDT	Frankfurt University		Federal Republic Germany
Prof. G.M. FARA	University of Milan		Italy
Dr. L. KARHAUSEN	E.E.C.	Paris Brussels	France Belgium
Prof.E.G. KNOX	University of Birmingham		United Kingdom
Prof. E.F. KROHN	University of Odense		Denmark
Prof. M.F. LECHAT	University of Louvain	Brussels	Belgium
Prof.C.R. LOWE	University of Wales	Cardiff	United Kingdom
Dr. R. MACLENNAN	C.I.R.C.	Lyon	France
Dr. K. MAGNUS	Institute Cancer Research	Oslo	Norway
Prof. L. MASSE	School of Public Health, Rennes		France
Mr. D. RABE	E.E.C.	Brussels	Belgium
Dr. P. RECHT	E.E.C.	Luxembourg	G.Duché Luxembourg
Dr. C. RUMEAU-ROUQUETTE	I.N.S.E.R.M.	Paris	France
Prof. R. SARACCI	C.I.R.C.	Lyon	France
Dr. W.M.J.VAN DUYNE	Ministry of Health and Social Security	The Hague	Netherlands
Dr.J.A.C.WEATHERALL	O.P.C.S.	London	United Kingdom

Members of Workshop. March 24th-25th 1975. Brussels.

Dr.Med.J.CLEMMESEN	Finsen Institute	Copenhagen	Denmark
Dr. G. DEAN	Medico Social Research Board	Dublin	Ireland
Dr. L. KARHAUSEN	E.E.C.	Brussels	Belgium
Dr. M.F. LECHAT	U.C.L.	Brussels	Belgium
Dr. C. RUMEAU-ROUQUETTE	INSERM	Paris	France
Dr.J.A.C.WEATHERALL	Office of Population Censuses and Surveys	London	United Kingdom

Absent - Dr. K.H. DEGENHARDT
Prof. E.G. KNOX

APPENDIX Ib.

VISITS MADE DURING FEASIBILITY STUDY 1975-1976

Country	Centre	Date	Visits conducted or reports prepared by
Denmark	Odense	October 3-4 1975	M.F.L., G.D., J.A.C.W., L.K.
	Copenhagen	February 1976	G.D.
Germany	Frankfurt (Bad Neuheim)	October 1975	M.F.L., J.A.C.W.
Belgium		No special visits	M.F.L.
France	Paris	January 1976	M.F.L.
	Brittany	January 1976	I.B.
	Lyon	January 1976	R.R., M.F.L., I.B.
United Kingdom	Liverpool	March 16th 1976	M.F.L., J.A.C.W.
	Belfast (in London)	March 9th 1976	J.A.C.W.
	Glasgow	March 16th-17th 1976	J.A.C.W., M.F.L.
	Aberdeen	January 16th 1976	M.F.L. & L.K.
Italy	Milan	April 21st-22nd 1976	M.F.L. & J.A.C.W.
	Firenze	August 1977	M.F.L. & L.K.
Ireland		No special visits	G.D.
Sweden	Stockholm	February 1976	G.D.
Norway	Bergen-Oslo	February 1976	G.D.
Finland	Helsinki	February 1976	G.D.
Iceland		CANCELLED	
Austria	Vienna	16th-17th February 1977	J.A.C.W.
Israel	Jerusalem	February 1976	M.F.L.
	Rehovoth		
Luxemburg		3rd August 1977	M.F.L. & I.B.
Yugoslavia		August 1976	G.D.
Netherlands	Leidenscham	23rd June 1976	M.F.L.
	Groningen	20th August 1976	M.F.L.
Germany	Munster	July 1976	M.F.L.

M.F.L. = Professor Michel F. Lechat, G.D. = Dr. Geoffrey Dean, I.B. = Dr. Irène Borlée, J.A.C.W. = Dr. Josephine Weatherall, L.K.= Dr. Lucien Karhausen, R.R. = Dr. Rumeau-Rouquette.

APPENDIX II.

MEMBERS OF EUROCAT COMAC - 1978-1981.

Belgium	Professor M.F. LECHAT (Chairman)	Catholic University of Louvain - Brussels.
	Professor R. BECKERS	Ministerie van Volksgezondheid en van het Gezin - Brussels.
Denmark	Professor M. HAUGE	University of Odense.
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	Dr. J. FEINGOLD	Groupe de Recherches de Génétique Epidémiologique - INSERM, Paris.
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The Netherlands	Dr. W.M.K. VAN DUYNE	Instituut voor Preventieve Gezondheidszorg - Leischendam
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	Prof. R.W. SMITHELLS	The University of Leeds.

APPENDIX III

CLASSIFICATION OF CENTRAL NERVOUS SYSTEM CONGENITAL ANOMALIES*

Condition	Definition	Variants	Synonyms**
ANENCEPHALUS AND SIMILAR ANOMALIES			
Acephalus	Absence of head		Acrania Acephalic monster Acephalia (Absence of brain) (Agenesis, aplasia of brain)
Anencephalus	Partial absence of brain tissue and of cranial vault; eyes and face present	Incomplete	Hemianencephaly Hemicrania Hemicephaly Meroacrania
		Complete	
		Cranio-rachischisis	Total dysraphism, (Amyeloencephalus)
Iniencephalus	Anomaly of foramen magnum and cervical vertebrae with retro-flexion of head and absence of neck groove	May be associated with anencephaly, spina bifida, microcephaly, hydrocephalus and encephalocele	Closed and open iniencephaly
SPINA BIFIDA			
Spina bifida occulta	Only one vertebral arch involved	Uncomplicated	
	More than one arch involved with widening of spinal canal, with or without dermal sinus, lipoma, dermatological or neurological lesion	Complicated	

* Reprinted from Nevin and Weatherall 1983 with permission of E.E.C.
** See notes at end of table

Condition	Definition	Variants	Synonyms*
Spina bifida cystica	Cystic extension of meninges, with or without neural tissue, outside the vertebral canal		Spinal hernia (Imperfect closure) (Hydrocele spinal)
		Meningocele (only meninges)	Hydromeningocele Congenital hernia dura mater
		Myelocele (meninges and neural tissue involved)	Spina bifida aperta (Hydromyelocele), Rachischisis Meningomyelocele, Myelomeningocele Myelocystocele, Myeloschisis
OTHER CONGENITAL ANOMALIES OF NERVOUS SYSTEM			
Cranial meningocele	Cystic expansion of meninges outside the cranium; does not contain brain tissue		Cerebral hernia Imperfect closure skull, Cranium bifidum cystica (pericranial sinus) Cerebral meningocele, (sinus/fistula pericranii)
Encephalocele	Cystic expansion of meninges outside the cranium, containing brain tissue		Hydroencephalocele Hydroencephalo-meningocele Cephalocele Encephalo-meningocele Encephalomyelocele Congenital hernia brain Congenital hernia of foramina Congenital cerebral hernia Hernia cerebral endaural Meningo-encephalocele

* See notes at end of table

Condition	Definition	Variants	Synonyms*
Microcephalus	Reduced size of brain with skull circumference less than 3 standard deviations below mean for age	It may be associated with a variety of other brain anomalies	(Hydromicro-cephaly), (microencephalon) (brain hypoplasia) (cephalic hypoplasia) (non-development of brain), (agenesis of skull and skull bones) Microcephaly
Agenesis of corpus callosum	Total or partial absence of the callosal commissure; other parts of the brain being present		Absence, agenesis, hypoplasia or aplasia of corpus callosum
Absence of cerebellum	Varying degrees of hypoplasia		Aplasia, agenesis, reduction deformity, hypoplasia or non-development of cerebellum
OTHER CONGENITAL ANOMALIES OF NERVOUS SYTEM (cont.)			
Lissencephaly	Unilateral or bilateral reduction or absence of the cerebral convolutions		Agyria Partial or total absence of cerebral gyri Pachygyria Hypoplasia of brain gyri
Micropolygyria	Reduction of the size and increase in number of cerebral gyri		Microgyria Polygyria
Arhinencephaly	Absence of the first cranial (olfactory) nerve and tract	A spectrum of anomalies from normal brain (except for absence of first nerve and tract) to single ventricle (holo-prosencephaly)	Alobar holopros-encephaly Cebocephaly, Ethmocephaly Cyclopia Cyclops

* See notes at end of table

Condition	Definition	Variants	Synonyms*
Ulegyria	Normal cerebral gyral pattern with atrophic sclerotic gyri		Distortion of gyri Walnut brain
CONGENITAL HYDROCEPHALUS			
Congenital hydrocephalus	Dilatation of ventricular system not due to primary atrophy of the brain, with or without enlargement of the skull		Communicating or non-communicating internal hydrocephalus, obstructive or non-obstructive hydrocephaly, (congenital macrocephaly)
		Blockage of aqueduct of Sylvius	Atresia, anomaly, obstruction, atresia, septum, stenosis, stricture, occlusion of aqueduct with congenital hydrocephalus
		Blockage of foramina of Magendie or Luschka	Blockage foramina 4th ventricle, atresia, obstruction, stricture, occlusion
		Blockage of foramina of Monro	
		Blockage of basal cistern	

* See notes at end of table

Condition	Definition	Variants	Synonyms*
		Others Unspecified	Hypoplasia, imperfect closure of skull or skull bones, degeneration of brain, distortion of skull or skull bones, anomaly skull or skull bones
Hydrencephaly	Bilateral absence of most of cerebral hemispheres. Particularly the fronto-parietal lobes are reduced to a translucent membrane enclosing cerebrospinal fluid		Hydrancephaly (Agenesis of cerebrum)
Arnold-Chiari Malformation	Downward displacement of the cerebellar tonsils through the foramen magnum into the cervical canal, associated with elongation distortion and downward displacement of the medulla oblongata and 4th ventricle		Types I and II Displaced brain Caudal displacement of brain
Dandy Walker Malformation	Cystic dilation of the fourth ventricle with midline cerebellar defect		
OTHER SPECIFIED ANOMALIES OF BRAIN			
Megalencephaly	Pathological hypertrophy of the brain	Hemimegalencephaly	Enlarged brain (Macrocephaly) (Macrogyria)
Porencephaly	Unilateral or bilateral cavities involving the full thickness of the tissue of the cerebral hemisphere		Porencephalic cyst Schizencephaly Single cyst Intracranial congenital cyst

* See notes at end of table

Condition	Definition	Variants	Synonyms*
Multiple cerebral cysts	Multiple cysts mainly confined to the white matter and usually not communicating with the ventricular system		Multiple periventricular cysts Leukomalacia Spongy brain (Ectopic cerebrum)
Other specified anomalies of brain			Colloid cyst of third ventricle Heterotopia Malposition Congenital softening (distortion) Progressive degeneration of brain Haematocephalus
OTHER SPECIFIED ANOMALIES OF SPINAL CORD			
Caudal regression syndrome	Absence of variable length of lower end of spinal cord		Atelomyelia
Diastematomyelia	Duplication of spinal cord always associated with spina bifida		Double or duplication of spinal cord Diplomyelia
Other lesions of cauda equina			Anomaly of cauda equina Defect of cauda equina
Syringomyelia	Cavitation of spinal cord predominantly in upper region		Dilatation of spinal cord Hydromyelia
Split notochord	Maldevelopment of vertebral bodies allowing variable neural and visceral elements		Neurenteric cyst Spinal teratoma
Other specified anomalies			Myelodysplasia Hypoplasia Micromyelia Aplasia, agenesis of spinal cord

* See notes at end of table

Condition	Definition	Variants	Synonyms*
OTHER SPECIFIED ANOMALIES OF NERVOUS SYSTEM			
Congenital cranial nerve anomalies	Specific nerve involvement, excluding arhinencephaly		Agenesis, aplasia, distortion, atrophy hypoplasia, entrapment by meningeal bands, bone or vessels Nuclear aplasia, of cranial or spinal nerves (midposition)
Optic nerve			
Acoustic nerve			
Congenital spinal nerve anomaly			
Meninges anomalies			Congenital (cerebral and spinal) adhesions, cysts or malposition of brain tissue Heterotopia cerebralis
UNSPECIFIED ANOMALIES OF BRAIN, SPINAL CORD & NERVOUS SYSTEM			
Unspecified anomalies			Distortion, deformity, anomaly malformation (Encephalopathy)

Notes

Riley Day syndrome
Marcus Gunn syndrome
Familial dysautonomia

Classify these with syndromes or in appropriate organ system

* Items in brackets under synonyms are rarely used. It is suggested that these terms should not be used.

APPENDIX IV

REGISTRY LEADERS AND THEIR ADDRESSES IN 1981

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Other EUROCAT Publications

— EUROCAT GUIDE FOR THE REGISTRATION OF CONGENITAL ANOMALIES. N° 1.
Edited by Philippe De Wals, Pierpaolo Mastroiacovo, Josephine A.C. Weatherall, and Michel F. Lechat.
1983.

Available on request to the Department of Epidemiology, Catholic University of Louvain, Clos Chapelle-aux-champs 30, 1200 Brussels, Belgium.

— REGISTRATION OF CONGENITAL ANOMALIES IN EUROCAT CENTRES 1979-1983.
Edited by Philippe De Wals, Josephine A.C. Weatherall, Michel F. Lechat.
Published by : CABAY, Agora 11, 1348 LOUVAIN-LA-NEUVE, Belgium.

The beginnings of EUROCAT tells how a cooperative scientific study in the epidemiology of congenital anomalies was set up within Member States and coordinated under the medical research program of the European Community.

The study is carried out through local registers which collect and record data about every child born with a congenital anomaly to any woman resident in a defined geographic area.

The first part of the book traces the development of the study from the first ideas early in 1972 through various committees and workshops to its commissioning in 1978. The second, and longer, part of the book considers some of the problems in establishing a multicentre study in Europe, and goes on to review the methods used and the progress made in the first four years. Starting from five working registers, each with its own methods in 1978, the study developed by 1981 to a coordinated set of 17 registers using common definitions and practices, together surveying over 200,000 births annually.

250 FB.

ISBN 2-87077-308-0