

Public health

North–South twinning in paediatric haemato-oncology: the La Mascota programme, Nicaragua

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We describe the La Mascota twinning programme between La Mascota paediatric hospital in Managua, Nicaragua, and hospitals in Monza and Milan, Italy, and Bellinzona, Switzerland. The programme was based on the belief that an attempt to reduce the gap in mortality from cancer in childhood between developed and less developed countries should become an integral part of the care and research activity of a haemato-oncological department of a developed country and not simply an exercise in solidarity. This programme for acute lymphoblastic leukaemia shows that intellectual, organisational, and financial resources can be generated by a twinning programme. What is vital for such programmes is a long-term commitment to a comprehensive and holistic strategy that incorporates supply of drugs, training and supervision of health professionals, and the care of the children and of their parents.

The health of children has become an indicator of the widening inequality between developed and less developed countries and of the human costs of economic development.^{1–3} Statistics of morbidity and mortality from preventable causes in children represent a measure of the socioeconomic and health-care performance of individual states and of their comparative ranking in international reports.^{4–7} Much attention is given to policies and tools that aim to control the most common diseases, which account for the greatest proportion of the global burden of disease. The inequality gap extends, however, to many other clinical conditions that are numerically less common, but share the same qualitative importance. Failure to treat avoidable life-threatening diseases represent a violation of the fundamental rights of children and of the professional duties of the health-care community.

Available data provide evidence that the overall incidence of childhood cancer in developing countries is broadly superimposable on that of developed countries.⁸ Childhood acute lymphoblastic leukaemia is a model scenario: its cure rate is as high as 70% in developed countries. No reliable data are available for countries with limited resources where most cases occur; in such countries the diagnosis of acute lymphoblastic leukaemia is rarely made and few children receive adequate treatment (table 1).^{10–12}

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Operational plan of La Mascota programme

The La Mascota programme was set up in 1986; it is a twinning programme between La Mascota paediatric hospital in Managua, Nicaragua, and hospitals in Monza and Milan, Italy, and Bellinzona, Switzerland. Nicaragua has a population of about 4 million people who live in an area of around 130 000 km². A fourth of the entire population lives in the capital city of Managua where La Mascota is situated; it is the only paediatric hospital in Nicaragua. The La Mascota project started when Nicaragua entered the most troubled phase of the Sandinista experience. During this period, the economic and military pressure imposed by US backed internal guerrilla and illegal economic embargo threatened the progressive plans of the Sandinista Government to provide basic health services to the whole population. The Italian-Swiss group was one of many non-governmental organisations that gave support to various sectors of the Nicaraguan health-care system at this time.^{13–16}

The idea of introducing acute lymphoblastic leukaemia among the traditional targets of cooperation came from the then director of the La Mascota hospital, a paediatrician and poet, Dr Fernando Silva, and the main group of the Italian-Swiss cooperation. The project was based on the hypothesis that the adoption of a disease such as acute lymphoblastic leukaemia could become not only a challenging way to tackle preventable deaths, but could also symbolise hope in a disheartening situation. The La Mascota project was conceived and promoted from the start as a research protocol, with well-defined rules for a twinning programme to which all participants had to comply (panel 1).

Year	Population ($\times 10^6$) of countries		Number of tumours in children per year	
	Developed	Less developed	Developed	Less developed
1970	1054	2643	35 000	115 000
1980	1146	3303	34 000	136 000
1990	1221	4071	33 000	151 000
2000	1286	4964	33 000	177 000

Data are from ref 9.

Table 1: Number of children with cancer in developed and less developed countries

Panel 1: Rules for a cooperative twinning programme

- Individuals from both sides, who are seeking change or looking for reciprocal promotion and autonomy, encouraged to take part in project.
- A comprehensive disease-orientated approach that includes training, supply of basic resources, strengthening of structural facilities.
- Long-term planning (minimum 5 years), with periodic reassessments and adjustments of strategies and needs.
- Clearly defined and progressively implemented policy of transfer of management responsibilities to local professionals.
- Cooperative adaptation and tailored adoption of the most important international protocols and guidelines as a teaching and planning tool.
- Financial support (in the donor pool) from diverse sources to enable the independence and flexibility of the project.
- Early involvement of community and parents' representatives to allow effective identification of needs and priorities.
- Ensure transparency of all project activities with periodic reporting to supporting groups.
- Establishment of research projects (with ad-hoc financial support) to further motivate the professional groups and encourage broader cultural interest.

According to a design that closely followed the methodology of a twinning programme, in which both sides have active complementary roles, the following local organisations were created in Nicaragua: Liga Nacional Contra la Leucemia y el Cancer en el Niño; Comision Nicaraguense de Ayuda al Niño con Cancer; CONANCA; and Asociacion de Padres de Niños Con Leucemia y Cancer. At the same time, the twin organisations were created in Italy to share with the Nicaraguan team the responsibility for funding, administration, and setting the priorities for further investments.

The training of a core group of medical doctors and nurses was the first step of the project, which was made possible by private financial support centred around the two clinical groups. During the 12 years of the project, six pediatricians, seven nurses, one pathologist, and two laboratory technicians from La Mascota were trained mainly in Monza and Milan, Italy, and partly in Bellinzona, Switzerland. The training was kept to a minimum, about 1 year, because we aimed to assess the immediate practical value of the skills in the difficult conditions of Nicaragua. Regular visits for supervision at La Mascota and further training were assured by the Italian and Swiss groups.

Outcomes of La Mascota programme

A striking result of the programme was that all the people who were trained, returned to and still work at La Mascota, despite the unstable economic and institutional conditions of Nicaragua. This outcome reflects the careful selection of the individuals who were chosen by the hospital director, the experience of taking part in a professionally rewarding activity, and the commitment fostered by provision of financial support for permanent education and travel opportunities for hospital staff.

As soon as acute lymphoblastic leukaemia could be diagnosed and induction treatments started, it became clear that one major obstacle to the successful

implementation of the programme was the absence of minimum structures for provision of adequate stay in hospital, for lodging the parents of children, and for outpatient care because of logistic and economic difficulties. The construction of two clean pavilions (ten beds each for haematological diseases and for solid tumours), of an outpatient clinic and of a parent house was made possible through the support of the groups in Italy and Switzerland. These groups provided additional funds beyond what had been planned for the provision of drugs and laboratory facilities.

The solutions adopted to tackle the difficulty of family participation in the process of care is an interesting result of the programme. Our approach was tailored to the living conditions of each child which were assessed with the support of a social worker, and incorporated length of hospital stay, use of the parents' house, and need and provision of money for transport to overcome the delicate balance between the long absences of a parent or the isolation of the child from the family.

The clinical and epidemiological results of the programme for diagnoses and treatment are shown in table 2. Compared with developed countries, childhood acute lymphoblastic leukaemia in Nicaragua has a similar distribution of lymphophenotypes. The main difference is that the 2–5 year frequency peak in Nicaragua is lower than in developed countries.¹⁷ The data start from 1990, when the first fully trained team had returned to La Mascota, to allow the activation and management of basic diagnostic and therapeutic protocols for acute lymphoblastic leukaemia. This protocol included standard morphological and cytochemical assessment of bone-marrow aspirates¹⁷ and the full treatment schedule (usually up to 2 years), with an in-hospital (up to 1 month) and an outpatient phase. Although acute lymphoblastic leukaemia was the core of the programme, it is clear that the interests and the competences of the staff expanded gradually to include most forms of childhood cancers.

A major part of the twinning programme was the orientation to ensure that cooperation was not simply an exercise of transferability of established diagnostic and therapeutic protocols, but rather part of research aimed at adaptation and assessment of the protocols in the specific conditions of Nicaragua. This research-oriented approach was not limited, however, to technology transfer. As soon as the minimum requirements of quality of routine care were assured, the Nicaraguan team was fully involved in more formal research projects that led to the joint authorship of scientific papers.^{17–22} The key issues and findings suggest what the outcome could be in terms of public health and general knowledge if the actors and the targets of research were extended beyond the present small fraction (about 20%) to the whole population of children with cancer. The increasing number of Nicaraguan children included in the programme—which expanded to include other areas of haematological disorders such as aplastic anaemia and to other paediatric fields such as urology, nephrology, and cystic fibrosis—inspired new forms of regular financial support. Such support was especially important because of the absence of response from institutional bodies and the steadily worsening social conditions in Nicaragua where the neo-liberal model of the new government was giving health less importance and funding than had previously been provided by the Sandinista Government.¹⁶

Neoplastic disease	Number of new cases by year								Number of cases of therapy*	Total
	1990	1991	1992	1993	1994	1995	1996	1997		
Acute lymphoblastic leukaemia	27	27	36	40	34	51	45	45	79	305
Non-lymphoblastic leukaemia	06	07	07	04	06	12	11	08	09	61
Non-Hodgkin lymphoma	06	05	05	12	11	10	17	10	40	76
Hodgkin's disease	05	03	05	17	08	07	08	08	34	61
Wilms' tumours	02	03	08	07	03	09	05	06	30	43
Retinoblastoma	01	—	01	11	04	08	05	02	14	32
Langerhans cell histiocytosis	01	02	01	07	02	03	03	04	17	23
Osteosarcoma	—	—	—	—	01	03	03	08	03	17
Neuroblastoma	—	—	—	—	02	02	02	01	02	07
Rabdomiosarcoma	—	—	01	02	03	04	06	04	03	20
Others	—	—	01	03	20	16	12	09	08	61
Total	48	47	65	105	94	115	117	105	239	706

*Off-therapy defined as patients who completed recommended treatment schedules and were judged cured for the index disease. The time and the probability to achieve this endpoint differ from one cancer to another.

Table 2: **Distribution of new children with neoplastic diseases diagnosed and treated at La Mascota hospital in 1990–97**

The concept of twinning was extended to include a programme of individual adoptions, whereby each child with a new diagnosis and his or her family was adopted for treatment by a twin family from Italy or Switzerland (cost per child of US\$ 1400). This programme was combined with initiatives that reduced the frequency of early interruptions of treatment from 30% to 5% of the cases, and stimulated the participation in fund raising of the local organisations mentioned above. This integration

Panel 2: **Extracts from the Montevideo statement**

The current situation

- When adequately treated, 60–70% of childhood cancers are currently curable.
- Today only 20% of the children worldwide benefit from adequate state-of-the-art therapy.
- 80% of the world's children—ie, those in countries with limited resources—are denied a cure.
- Cancers represent the first disease-related cause of death among children in developed countries (second only to accidents). Mortality from childhood cancer is the third or fourth cause of death among children in many of these developing countries.
- Childhood cancer is increasingly important in countries with limited resources, because of the substantial increase of children in the population as a result of the high birth rate and of the decreased mortality from communicable diseases or malnutrition.
- Mortality from childhood cancer could be reduced by the establishment of paediatric hematology-oncology programmes with centres that provide free essential therapy to all children who need treatment.
- The implementation of such programmes should be considered as a step towards the application of the United Nations Convention on Children's Rights (New York, Nov 29, 1989).

We therefore request that Governments and international financial bodies:

- Take into consideration the issue of paediatric oncology in countries with limited resources.
- Undertake initiatives and allocate resources for the implementation of paediatric oncology care and research programmes.

As representatives of the family of paediatric oncology we commit ourselves, and propose:

- To foster all activities that may contribute to the mobilisation of the community at large towards programmes of international cooperation.
- To promote the systematic implementation of centre-to-centre cooperation as a concrete contribution to the respect of the neglected rights of children.

of new sources of financial support allowed us to cope with the increasing cost of diagnostic procedures and drugs after 1996.

The outcomes of the La Mascota programme were so encouraging that the potential expansion of the twinning programme seemed to be the next step. After various exchanges with colleagues from different parts of the world, a consensus document was presented at the XXVII Meeting of the International Society of Paediatric Oncology (SIOP), which was held in Montevideo in 1995. This document (The Montevideo Statement, panel 2), proposed that each advanced centre of the North should consider becoming a twin of a centre in the South, and was approved by SIOP in 1997.²¹ To further promote and articulate this perspective and symbolise the evolution of the idea on its tenth anniversary, in September 1996, the Monza's International School of Pediatric Hematology-Oncology (MISPHO) was launched. MISPHO invited two representatives of each of 14 countries of Caribe, Central and South America (Bolivia, Colombia, Costa Rica, Cuba, Ecuador, El Salvador, Guatemala, Honduras, Nicaragua, Paraguay, Perú, Dominican Republic, Uruguay, Venezuela) to a 2 week intensive course. This course aimed to: revise the diagnostic-therapeutic protocols and the conditions of organisation of care for acute lymphoblastic leukaemia in the participating countries; to assess the relevance and the transferability of the model adopted in Nicaragua, where the most successful protocols of the leading world centres had been adapted to become applicable with an acceptable risk and cost-benefit profile; to propose and adopt a strategy of networking among the various countries represented in the course; and to assess whether

	Funding (US\$ × 1000)*			
	1986–89	1990–93	1994–97	Total
Antineoplastic drugs	30	200	200	430
Training and fellowships	40	220	220	480
Physical structures	—	130	60	190
Laboratory	—	50	30	80
Psychosocial support†	—	20	200	220
Total	70	620	710	1400

*Funding from: Comitato M L Verga, M Tettamanti Foundation, Monza, Italy; Associazione per l'Aiuto Medico al Centro America, Bellinzona, Switzerland; solidarity groups; governments; adoption programme from Italy, France, and USA. In 1998 a 12-bed ward (cost of US\$ 700 000) was donated by the Ducate of Luxembourg.

†Includes full-time salary of social worker and psychologist, together with financial support for the families.

Table 3: **Distribution and sources of funding by institutions and solidarity groups from Italy and Switzerland for La Mascota programme**

the twinning strategy that was the core of the Montevideo declaration could be generalised. This last objective was specifically explored through the involvement of representatives of some of the leading groups in the field of paediatric oncology.

A final, mandatory, note is the cost of the whole operation (table 3). There is little doubt that the investments seem to be highly effective. In addition to the free provision of facilities to people who would otherwise not have such opportunity, our data indicate a cure rate of about 50% for acute lymphoblastic leukaemia (unpublished data) and 80% for Hodgkin's disease.²⁰

Discussion

The purpose of this report is not to look backwards to the success of this project, but to formulate hypotheses for the future. The lessons of the La Mascota programme and its promising development is to show that the gap between resources and their availability where they are most needed can be bridged.²² Although the direct structural involvement by official national and international bodies is obviously needed (and must be sought), it is realistic to behave as if such involvement might not occur. Indeed, most trends in health care seem to go in the opposite direction; resources for expensive advanced interventions will inevitably be restricted to the few who can pay for them. Moreover, most children from less developed countries already have to fight hard for the basic needs of nutrition, vaccination, essential drugs, and the most frequent causes of morbidity and mortality.⁶⁻⁷

The scenario of twinning programmes between centres in developed countries with advanced resources and reference groups in poorer countries might seem to be a proposal inspired by an illusory sense of solidarity. However, the twinning approach is a realistic challenge and duty for those who work in the most advanced frontiers of childhood cancers. The outcome of the most intensive protocols should in fact be assessed not simply against the small denominators of the groups of children included in the recommended or research protocols, but against the much broader issue of the incident cases in countries where the cure rates, unacceptably low (table 1).

Our experience shows that intellectual, organisational, and financial resources can be generated if a group includes among its research priorities and criteria of quality of care the establishment of a twinning programme. Far from competing with the group's own projects and development, an orientation in this direction is stimulating, because it favours a permanent reassessment of what is valuable and essential, and what can and must be adapted and streamlined.^{21,22} The response of the institutions involved in the twinning programme seems to be positive, despite unfavourable conditions, and has become an effective cooperation between peers. What is vital is a long-term commitment to a comprehensive strategy that is not limited to only one part of care (supply of drugs, training, or supervision).

The La Mascota programme for childhood acute lymphoblastic leukaemia, and its extension to general paediatric oncology, is a model case. This approach should be applied to other specialistic programmes; the

responsible transfer of effective interventions cannot wait for future unspecified economic developments. The adoption by international professional organisations of position such as the one formulated in the Montevideo Statement²⁰ could help to create favourable cultural and policy attitudes that will encourage an increasing number of groups to take part in this much needed approach.

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