

CURING PAEDIATRIC CANCER IN THE DEVELOPING WORLD

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As cancer emerges as a significant threat to life in low- and middle-income countries, targeted external aid through genuine twinning partnerships can make a difference. The local medical/nursing teams must determine the aims and objectives and the role of outsiders is to provide mentorship, advocacy and support based on the experiences we have gained from the advances made in high-income countries.

One of the remarkable success stories of the last 4–5 decades has been the improvement in survival for children with cancer from little chance of cure to 75–80% long term survival in 2012¹. However, of the 160–200,000 children who develop cancer worldwide annually, access to diagnosis and care is barely 20%^{2,3}. Consequently at least 100,000 die each year undiagnosed or untreated and most receive no relief of their symptoms^{3,4}. Yet many childhood malignancies are sensitive to relatively cheap cytotoxic regimens (eg Burkitts lymphoma, neuroblastoma, retinoblastoma). Cure for many children is possible⁴. How can we rectify the inequality of care and “chance of life” between those living in high (HIC) and low- and middle-income (LMIC) Twinned programmes linking high- and low-income countries have shown that improvement is achievable provided that there is a long term supportive commitment to the project^{5,6,7}. It is essential to have strong local medical and nursing leadership and there must be “buy in” from hospitals, ministries, non-governmental organizations (NGOs) and some local philanthropists. Only then can there be development with long-term sustainability.

Table 1 shows the obstacles to be overcome in starting the treatment of young people with cancer. It is crucial to understand these challenges and for oncologists, and all who care for children worldwide to find solutions and work together to make them real in the interests of children worldwide.

Poverty

Sadly childhood cancer emerges as a significant threat to life as socioeconomic conditions improve and deaths from communicable diseases begin to be controlled.

Table 1: Obstacles to be overcome in starting the treatment of young people with cancer

Challenges to overcome

- Individual family, community, national poverty
- Other overwhelming societal priorities
- Natural and man-made disasters
- Lack of cancer incidence registration
- Lack of awareness /perceptions of incurability
- Lack of access to diagnosis/treatment
- Lack of palliative care
- Lack of trained staff/ability to retain staff
- Infrastructural problems e.g. transport

The strongest correlation for childhood cancer survival in the first 10 countries supported in the “My Child Matters” initiative⁸ was annual governmental health care expenditure ($r^2 = 0.882$, $p < 0.001$) which also correlates with gross domestic product and numbers of doctors and nurses/1000 population⁹.

When parents can barely afford to feed their family, the cost of cytotoxics, supportive care, hospital visits; and the consequent loss of earnings when a key family member has to be away with the child in hospital, the financial burden of cancer is totally prohibitive. As a result treatment refusal, and “abandonment” are a high risk. Abandonment rates vary widely, 1–60%, depending on where the family live¹⁰. The rates have been reduced; by families being convinced that a “cure” is possible¹⁰, by increased government funding specifically for care (e.g. in Mexico) and subsidized cytotoxics as part of a twinning partnership¹¹. The ultimate goal must be to promote long-term sustainability within each country with funding from governmental monies, local NGOs and philanthropists.

The distance families have to travel to receive care also

Table 2: Trends in under 5 mortality 1990 – 2008 (rates/1000 live births)

Region	Fall in deaths	% reduction	% of all deaths worldwide
Africa	168 – 132	21%	51%
Sub Saharan	184 – 144	22%	50%
N Africa/Mid East	77 – 43	44%	5%
Asia	87 – 54	38%	42%
South Asia	124 – 76	39%	32%
East Asia/Pacific	54 – 28	48%	9%
Latin America + Caribbean	52 – 23	56%	3%
Industrial countries	10 – 6	40%	1%
Least developed countries	179 – 129	28%	40%

Data derived from You D et al Lancet 2012¹⁶ and <http://www.childmortality.org> 20/8/2009¹⁷

influences compliance with treatment¹². Development of satellite clinics closer to areas of population has helped. Accurate and clear communication to all parents irrespective of socioeconomic status also influences abandonment rates¹³. Realistically it is essential that for some years to come we need collectively to develop more affordable graduated intensity protocols¹⁴ to provide an affordable chance of cure in low-income countries.

Internationally those of us in HIC need to work harder to ensure that all children have access to and receive reliable supplies of low cost generic drugs¹⁵. This requires the involvement and collaboration of professional bodies, the World Health Organization and the pharmaceutical industry. The International Society of Paediatric Oncology (PODC Committee) has established a group to explore how this can be achieved.

Other overwhelming priorities

Table 2 shows the progress made in reducing under 5 mortality. Forty-two low- and middle-income countries account for 90% of all under 5 year deaths¹⁶. The target of Millennium Goal 4 was a reduction of 66% by 2015.

Programmes to reduce mortality from infections (especially malaria, measles, TB, HIV, diarrhoea) and malnutrition have been developed and generously funded. They are succeeding in many but not all countries. However too many high-income countries have reduced their overseas aid donations¹⁸. Despite the best efforts of the Non Communicable Diseases Alliance for Children and Adolescents, childhood cancer was virtually ignored by the UN High Level Meeting on NCDs in 2011. There has to be greater international and governmental focus on NCDs beyond 2015.

Disasters

Natural disasters (famine, floods, tsunamis, drought) distort and overwhelm fragile economics. Even more disastrous, are

war, civil or between countries. Women and children are always the first victims. During such crises external funding may become essential but cancer care is never a priority when there is civil chaos or unrest. To work effectively, aid given during crises, and certainly thereafter, needs to be channelled through local and national professionals in cooperation with the local community driven by their local evidence and experience, not by international “political expediency”. However very good clinical and financial governance must be in place and monitored. Activation and empowerment of parents, families and local communities have been the key to success in twinning cancer programmes^{5,6,7}.

Cancer registration/databases

It is essential to document all new cases (tumour type, stage, delays in diagnosis and treated/not) and to record their outcome. This is not only important for assessment of progress (individual and collective) but also to accurately plan service provision. Very few LMIC have true population-based registration schemes which are costly. WHO/IARC need to assist more countries to establish such registration. Meanwhile every developing unit needs to document its activity and ideally use a freely accessible database like POND¹⁹. If a developing centre starts to develop shared care/satellite centres then it progressively becomes a good surrogate for a population-based database.

Awareness/perception of curability

Missed and misdiagnosis as well as delayed diagnosis result from lack of both public and professional awareness of the meaning of clinical signs and symptoms of cancer. They result in late or no referral to a knowledgeable paediatrician and incurability of the cancer. Public lack of awareness and no belief in curability by conventional medicines leads to initial use of cheaper but ineffective traditional medicines^{20,21}. Twinning programmes emphasize the need to educate doctors

and nurses (both specialists and community paediatricians) as well as other health workers and the public. All of this requires an alliance with the local community^{5,11}. All awareness campaigns require the messages to be clear, repetitive and protracted to ensure a long term impact.

Access to diagnostics and drugs

There are three components which influence long-term survival; access to diagnosis, access to treatment and effective therapy. Because we have highly sophisticated investigative laboratory technology and imaging in HICs, it does not mean that they are essential for an adequate diagnosis. Twinning partnerships can provide technology transfer, remote confirmatory diagnostics and second opinions in complex cases^{19,22,23} but basic x-rays, ultrasonography and good routine pathology are adequate for many childhood tumours. Graduated intensity protocols should contain the basic essential diagnostics which can be added to as financial circumstances change³.

A consistent supply of affordable cytotoxic and supportive drugs for all children worldwide must be our aim, especially the necessary analgesics, including opiates to relieve pain. The World Health Organization (WHO) has produced and regularly revised an Essential Medicines List²⁴. In 1994 an expert committee listed 10 essential cytotoxics for childhood cancer, updated in 2007 to 19 (all generic and off patent). This "Essential" list is still complementary not substantial. All of these drugs could be produced, marketed and distributed at a more reasonable cost if there was the will to do so. Yet many of them are not consistently available even in the 156 countries who have signed up to the list. Pui et al⁴ proclaimed the Rights of children everywhere to potential curative therapy. Target 17 of Goal 8 of the Millennium Declaration stated the need for cooperation with pharmaceutical companies to provide access to affordable essential drugs in developing countries²⁵. If drugs are not on the Essential List most LICs will not permit their importation and/or local production. However all these drugs are on the Essential list but still not imported, or if they are, in inadequate amounts and are not made locally. More European pharmaceutical companies than American ones appear aware of the needs of developing countries²⁶. Greater coordinated activity is required to turn guidance into action. The greatest worldwide failure is to ensure availability of effective analgesia for suffering children. There is a stigma associated with prescribing, dispensing and taking therapeutic opiates in many countries based often around false beliefs about addiction. Until the medical world clarifies and dispels the myths around potent analgesics many hundreds of thousands

of children in particular will have painful and miserable deaths. WHO and governments worldwide need to play a greater part in resolving this issue. The ultimate irony is that those countries which grow the most opium poppies prohibit the use of medicinal opiates for their own population!

Staff training

WHO has repeatedly emphasized the need for careful training of staff if cytotoxics are to be delivered safely. Far too often doctors and nurses have gone abroad for such training and been recruited away from their country of origin. In-country essential training must be the norm with only short term travelling scholarships for specific training needs at an established cancer centre all arranged by contract and a guaranteed job on return. Retention of trained staff is critical to the success of a developing service. Too many excellent doctors and nurses have been lost to their own country and gained by high-income countries who should be training their own staff.

There are excellent models of successful, fully evaluated nurse training schemes in several LIC, especially those established by the St Jude Outreach team²⁷. Subsequent nurse subsidies to help retain such trained staff have been effective in Latin America and some centres in Africa.

Global collaboration by all involved in twinning partnerships would greatly enhance the equality of educational training and production of consistent advice and aids to learning.

Societal infrastructure

The difficulty of accessing specialist cancer services at a centre of expertise remote from where a family may live does contribute to abandonment of therapy and follow-up. Creation of shared care/satellite clinics aims to reduce (for some therapy and follow-up) the time and distance to reach care¹². Financial help with travel costs, good parental accommodation, welcome packs and nutritional supplements for both the patients and supportive family member(s) aids adherence to treatment and increases the chance of cure.

Conclusions

As cancer emerges as a significant threat to life in low-middle income countries, targeted external aid through genuine twinning partnerships can make a difference. The local medical/nursing teams must determine the aims and objectives and the role of outsiders is to provide mentorship, advocacy and support based on the experiences gained from the advances made in high-income countries. Global collaboration is required to address the multiple challenges

highlighted here. That collaboration requires some refocusing by professional medical and nursing organisations, parent groups, NGOs, WHO and governments around the world. Cancer and other noncommunicable diseases are becoming an increasing threat to life which cannot be ignored any longer. ●

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