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The Kenyan National Retinoblastoma Strategy: Building local capacity in the diagnosis and management of pediatric eye cancer in Kenya

By Helen Dimaras, PhD, Abby White, and Brenda Gallie, MD

As ophthalmologists practicing in Canada, we are fortunate to have at our disposal, the highest levels of health infrastructure and technology to maximize patient care. However, this is not the case in many parts of the world, especially in "developing" countries. We are encouraged to "give back to society" through using our clinical and teaching expertise to help those who cannot access appropriate healthcare resources. The University of Toronto has developed a Centre for International Health, and its Ophthalmology Department has a major focus on International Ophthalmology.

This inaugural International Ophthalmology article, written by the team of Dr. Brenda Gallie, one of the foremost retinoblastoma experts in the world, is an excellent example of how our expertise can be applied to help better the lives of patients in less fortunate healthcare environments.

Jeff Hurwitz, MD, FRCSC

Death from a delayed diagnosis of retinoblastoma is almost unheard of in developed countries, where 97% of patients are cured and the main focus of treatment is on preserving vision. The high cure rate achieved in resource-rich countries can be equally achieved in Kenya with minimal financial input, by building local capacity for improved diagnosis and management of retinoblastoma. This issue of *Ophthalmology Rounds* presents an overview of retinoblastoma care and management in Kenya, and the national strategy that is currently emerging.

Brief overview of retinoblastoma

Retinoblastoma is the most common eye cancer of infancy and early childhood. When fully confined to the eye, it is curable by surgical removal of the affected eye. Established treatments to preserve vision include focal laser and/or freezing therapy for small tumours, and systemic chemotherapy in combination with focal therapy for larger tumours. Genetic testing enables prenatal diagnosis in families at risk, supporting very early detection of tiny tumours and vision-saving treatment with laser and cryotherapy. Radiation is used as a treatment of last resort. Retinoblastoma that spreads beyond the eye is often fatal, even with intensive chemotherapy, radiation, and bone marrow transplant.

The global retinoblastoma disparity

Retinoblastoma survival is above 97% in resource-rich countries like Canada. A major Canadian research focus on retinoblastoma has contributed significantly to current optimal patient care. There is a clear understanding of the genetic basis in retinoblastoma initiation and progression, which has been applied to clinical diagnostic testing and exported to international families (www.retinoblastomasolutions.org).[1] Our group leads an international multicentre clinical trial designed to optimize chemotherapy for intraocular disease with retention of

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Table 1: Projected number of new retinoblastoma diagnosed each year, calculated from January 2006 population data, birth and infant death rates for each country, assuming 1/15,000 live births

Country Participants in World Survey	Total population (2006 est)	Birth rate	Infant mortality rate	Forecast births	Forecast retinoblastoma per year
India	**1,095,351,995**	**22**	**55**	**22,791,639**	**1,519**
China	**1,313,973,713**	**13**	**23**	**17,007,629**	**1,134**
Indonesia	245,452,739	20	34	4,820,816	321
Nigeria	131,859,731	40	97	4,813,227	321
European Union	456,953,258	10	5	4,546,228	303
United States	298,444,215	14	6	4,192,867	280
Mexico	107,449,525	21	20	2,178,090	145
Ethiopia					172
Kenya					86
France	60,786,136	12	4	726,832	48
Argentina	39,921,833	17	15	658,054	44
Spain	40,397,842	10	4	404,626	27
Canada	33,098,932	11	5	355,133	24
Australia	20,264,082	12	5	244,867	16
Switzerland	7,523,934	10	4	72,740	5
Finland	5,231,372	10	4	54,474	4
World	**6,525,170,264**	**20**	**49**	**129,057,443**	**8,604**

Data from https://www.cia.gov/library/publications/the-world-factbook/.

vision.[2] This protocol also has some success in the cure of extraocular disease;[3] however, these resources are only available to children in countries with significant expenditures in healthcare (generally associated with gross national product [GNP] per capita). Approximately 92% of children affected by retinoblastoma live in countries that are less economically developed (Table 1). While curative therapy for intraocular disease may be available in these countries, access to appropriate care for retinoblastoma is severely hindered by minimal awareness and the barriers created by endemic poverty (Table 2). Most children present with advanced disease, and global survival is estimated to be <20%.

Daisy's Eye Cancer Fund and Rati's Challenge

Our ophthalmology department became acutely aware of these discrepancies when Rati, a young child from Botswana, came to Canada for treatment of orbital recurrence, 1 year after enucleation for unilateral retinoblastoma. Pathological evidence of optic-nerve involvement had suggested the need for monitoring and chemotherapy. Rati's parents, however, learned this only when a recurrent tumour filled her orbit, and they sought help via the Internet. Rati received treatment in Toronto with help from Daisy's Eye Cancer Fund (DECF – www.daisyseyecancerfund. org), an organization founded by the family and friends of a young retinoblastoma survivor in England, who had also received treatment at SickKids Hospital. Rati's extensive intracranial disease responded well for only 2 years and when she died, Rati's Challenge was initiated in her honour within DECF, to address poor retinoblastoma survival in Africa.

A co-founder of DECF, Abby White, has deep roots in Africa. Her father was born in Kitale, northwest Kenya with bilateral retinoblastoma. He received life-saving bilateral enucleation and radiotherapy in England. Abby also received successful treatment for bilateral retinoblastoma; she often visits family in Kenya, she speaks Swahili and knows Kenya well. While Botswana expects only 2.4 new cases of retinoblastoma per year, Kenya has 86. The wider Eastern Africa region experiences 750 new cases per year; many of these children seek treatment in Kenya, since Nairobi is a major ophthalmic training centre for the continent. On short visits to Kenya in 2006 and 2007, University of Toronto staff met many dedicated and highly motivated people concerned about these children, and the Kenyan National Retinoblastoma Strategy (KNRbS) was born.

Retinoblastoma in Kenya

In Kenya and other developing nations, retinoblastoma kills approximately 80% of affected children. The 3-year survival rate of retinoblastoma patients treated at the Kenyatta National Hospital between 2000 and 2004, inclusively, is 26% .[4] Death is due to:

- late diagnosis when retinoblastoma has spread into the brain and/or bone marrow
- suboptimal application of resources due to delayed and incomplete pathology reports
- inadequate resources to support the family when costs of medical bills, travel to access treatment, lack of family accommodation near hospital, and fear of mutilation and blindness upon removal of the eye "force" abandonment of therapy.

Table 2: The top 30 countries in terms of money spent on health compared to all the other countries, and the mean GNP per capita, compared to the projected numbers of newly diagnosed retinoblastoma children each year

	Health expenditure		
	World rank top 30	World rank below 30th	Whole world
Forecast retinoblastoma	668 (8%)	7936 (92%)	8604 (100%)
Weighted GNP per capita (2006 US$)	34 111	7068	10 458
Population	876 m (12.5%)	6110 m (87.5%)	6986 m (100%)

Projected number of new retinoblastoma diagnoses each year are calculated from the January 2006 population data, birth and infant death rates for each country, assuming 1/ 15,000 live births.

GNP = gross national product

Data from the World Health Organization. World health report 2006 statistical index (www.who.int/whr/2006/annex/en/index.html), and Theodora economic data (www.theodora.com/wfb2006/spreadsheets).

Figure 1: The white tumour filling the left eye of this child on the T-shirt and poster distributed across Kenya was very effective in bringing attention to the important message (translated from Swahili): "A white reflection in a child's eye could be a sign of cancer! If your child's eye looks like the one in the photograph, make sure both eyes are checked by a medical doctor. Untreated, children's eye cancer is fatal, but when diagnosed early it is very curable! Don't be slow. Help your child to be a survivor!"

The most common early sign of retinoblastoma, a "white pupil" (Figure 1), is often missed or misdiagnosed at multiple levels (primary-care physicians, healthcare personnel, pediatricians, ophthalmologists, oncologists, parents, and the public). When cancer is contained within the eye, surgical removal of that eye is curative, requiring minimal stay in hospital. However, the intensive therapy required for treatment of extensive retinoblastoma due to late diagnosis places considerable burdens on the family and healthcare system, with generally unfavourable results. Lack of family accommodation near hospitals and high transport costs lead to medically unnecessary hospitalization of children to ensure adherence to therapy. This increases the medical bill and blocks beds needed by other patients. Total therapy costs are high, and often absorbed by the hospital when payment by the family is not possible. When the diagnosis is early, the costs of medical care are significantly lower and the burden on family and the local healthcare system is reduced.

The Kenyan National Retinoblastoma Strategy (KNRbS)

To optimize opportunities for curing children with retinoblastoma, DECF has launched a 5-year capacity-building project with Kenyan colleagues. The project aims to establish a sustainable, locally owned retinoblastoma healthcare program that can increase survival in this resource-limited setting to a level closer to that in countries like Canada. Following a "micro-loan" approach, it is expected that our small financial input will be repaid multiple times by the value-added results of a homegrown program. The KNRbS includes retinoblastoma experts in all relevant health fields, patients, parents, and dedicated local volunteers. This dedicated team has established a solid foundation for the project through DECF-Kenya, and is now a registered Kenyan nongovernmental organization (NGO) with a very active Board of Directors, chaired by Dr. Vijoo Rattansi, Head of the Rattansi Educational Trust.

Working together with the local community, increasing knowledge of retinoblastoma management and nationally coordinated awareness and care has been facilitated. In the process, resources already available in Kenya are being used to improve access to care for families currently overwhelmed by the costs of intensive therapy. This is a novel approach to the management of a rare disease in a resource-limited setting. Success in this venture could offer guidelines for improving the management of other rare diseases that are often overlooked, yet have a catastrophic impact on life in less developed regions of the world. When the measured effective impact of the KNRbS is clear, the retinoblastoma model can perhaps be deployed elsewhere.

KNRbS core components

Obstacle: Lack of coordinated care and communication

Independent efforts have emerged between resource-rich treatment centres in developed countries and resource-poor hospitals in less developed regions of the world to share knowledge and improve outcomes.[5] These "twinning" programs usually work on a case-by-case basis, and long-term benefit is dependent on development of teams in the resource-limited treatment centres. For example, in 2002, doctors at Kenyatta National Hospital in Nairobi established a Retinoblastoma Working Group to develop improved care at the centre. However, with limited personnel already stretched by increasing demands for care, little progress was made.

Telehealth is currently limited in Kenya because of poor Internet speed across the country. The high cost of international flights, compared with low physician salaries also renders professional development conferences inaccessible to most practitioners. Due to its rarity, minimal published literature is available regarding appropriate management of the cancer in resource-limited settings. Inconsistent and incomplete medical records, coupled with poor telecommunications between different treatment centres, results in poorly managed care and near absence of appropriate follow-up.

Solution: Develop the KNRbS

Modeled on the Canadian NRbS, DECF-Kenya is collaborating with the original Working Group and their colleagues across the country to develop a sustainable, locally managed diagnosis and treatment program. Lay volunteers (patients, parents, healthcare lawyers, health advocates, family-support groups, and politicians) are working together with professionals (ophthalmologists, pediatric oncologists, nurses, social workers, childlife specialists, and researchers in cancer biology, clinical studies, healthcare delivery, social sciences, informatics, and best-practice guidelines). The first KNRbS meeting was held from September 19 to 21, 2008, to determine the short- and long-term action items. This meeting was attended by 70 hard-working, determined Kenyans and DECF members, and funded by the Canadian Institutes for Health Research and the Sir Halley Stewart Trust in England through DECF.

The KNRbS will revise current methodologies and nurture intercentre cooperation to promote effective retinoblastoma care and family support structures. Strategic international links will be developed through an educational and consultative Internet Tumour Board. Close collaboration between Kenya's retinoblastoma treatment hub, Kenyatta National Hospital in Nairobi, and Canada's principal treatment centre at SickKids in Toronto will help optimize available resources and a realistic selection of treatment. The Canadian Retinoblastoma Guidelines will provide a framework for modification by the KNRbS to achieve common standards of care across Kenya. Developed under the leadership of the parent-led Canadian Retinoblastoma Society, these consensus recommendations will be adapted to address the very different issues confronting Kenyan families.

To address the incomplete record-keeping issue, the implementation of a national point-of-care database is proposed. Modeled on eCANCER-Care[RB], which supports care at SickKids for retinoblastoma patients, this database can be adapted for the Kenyan situation, and help standardize records and remind clinicians of agreed guidelines for treatment and follow-up. The data will essentially become a Kenyan Retinoblastoma Registry. By harnessing cellular Internet technology, data can be recorded from remote locations, improving follow-up and enabling children to return home promptly after treatment. It is also proposed to combine this technology with outreach eye camps that may provide a link for ophthalmological examination in children otherwise lost to follow-up. Annual meetings of the KNRbS will facilitate its development and evaluate the effectiveness. These meetings will promote local creativity and innovation, maximizing Kenyan-owned efforts and collaborative approaches.

Obstacle: Lack of retinoblastoma awareness

Lack of retinoblastoma awareness is the biggest hurdle to achieving the early diagnosis essential for survival. A white pupil (leukocoria) is the most common early sign of retinoblastoma worldwide (Figure 1). Noticed first by those caring for the child, and requiring no special equipment, leukocoria can be easily detected by the general public. However, early diagnosis requires that parents and primary-healthcare workers recognize that this sign can indicate childhood eye cancer and a threat to life. Presently, delays occur because parents are often unable to access health workers who are aware of retinoblastoma or an ophthalmologist familiar with its management.

Solution: Initiate a national retinoblastoma awareness campaign

A pilot Retinoblastoma Awareness Campaign has been carried out in Kenya, targeting both medical personnel and the public. In 2006, a DECF team from Canada (Brenda Gallie), the United Kingdom (Abby White), Ethiopia (Samson Tsegaye, parent), and Kenya (Brian Ouma) found tremendous local interest in a T-shirt and poster campaign highlighting the "white pupil" in early diagnosis of retinoblastoma (Figure 1). Describing in Swahili how early attention to such eyes can save lives, the campaign generated strong positive feedback from across Kenya.

A structured awareness campaign will include dissemination of educational posters to primary-health centres and through national infant-vaccination campaigns, since most cases of retinoblastoma arise in this age group. Posters, flyers, T-shirts, and audio-visual materials will be used to promote awareness and understanding of retinoblastoma among parents and the primary health- care community. Written materials will be provided to advance the training of medical professionals, enable informed decision-making by parents, and improve psychosocial support for

families. Each segment of the campaign will be monitored to assess the impact on early diagnosis and referral. The retrospective study conducted at Kenyatta National Hospital will be extended to the other major centres treating retinoblastoma. Moving forward, eCancerCare[RB] will record standardized classification of disease at presentation, delays from first signs, methods of treatment, and outcomes. These data will be evaluated to identify the effectiveness of the awareness campaign, particularly noting geographical or healthcare sectors where it fails and a different approach is needed.

Obstacle: Poor and inconsistent pathology service

To rule out metastatic disease, physicians must be certain there is no tumour activity in the optic nerve or outer layers of the eye. When surgical pathology confirms no risk factors for extraocular involvement, no further treatment is necessary. However, pathology reports in Kenya frequently confirm only that the pathological findings are consistent with retinoblastoma. As a result, reports indicating no risk for extraocular involvement are rarely trusted. Slow pathology reporting also places great pressure on doctors to further treat children with chemotherapy, on the basis that they *might* have tumour extension beyond the eye. As a result, children presenting with disease contained in the eye may be over-treated, sometimes with chemotherapy protocols that have no proven use in retinoblastoma care, due to inability to obtain the appropriate drugs. The most impoverished children are admitted to hospital to ensure adherence to therapy, denying them a free childhood and a positive family environment. For 58% of Kenya's population, daily earnings are less than US$2, and rising medical bills cripple many families. Children are not usually released from hospital until payment is received, thus, abandonment of treatment and child is common.

Solution: A nationally coordinated expert pathology service

DECF is working with local professionals to establish a coordinated national retinoblastoma pathology service that can provide expert review and accurate reporting in a timely manner for every child. Identifying children with a tumour extension at high risk for recurrence will enable optimal application of available resources, reducing inappropriate over- or undertreatment. In turn, this will relieve pressure on the healthcare system and reduce the burdens placed on families whose children do not require further therapy, or who will not benefit from further intensive treatment. The maxillofacial pathology unit at Nairobi University has pledged its services free of charge for 15 years for retinoblastoma children. In return, SickKids will provide training in comprehensive retinoblastoma pathology assessment and reporting for Elizabeth Dimba, BDS, PhD, a Kenyan pathologist. A microtome has been donated by the University Health Network, Toronto, to replace the antiquated unit presently used in Nairobi, enabling a safer and more effective working environment for retinoblastoma pathologists.

Figure 2: "Dr. Rati" practices sterile technique with Child-Life specialist, Morgan Livingstone. Child-life training empowered Rati to undergo 20 external-beam radiation treatments without sedation or chemotherapy

Obstacle: Lack of psychosocial support for families and children

Cancer treatment is a stressful and potentially traumatic experience that can overwhelm a child's ability to cope and cooperate with his or her doctors. This can inhibit healing and natural development, with lasting negative effects on the child's physical and mental health. Hospitalized children are often separated from their parents due to lack of parent accommodation at the hospital and the high cost of lodging in the city. Many parents are forced to sleep "rough" (on the street) to remain close to their child, or return home to care for other children.

Solution: Implement a childlife and family support program

Medical play, education, and self-expression activities based on natural child development underpin emotional well-being, compliance with therapy, optimal development, and successful integration into society. Increased cooperation from the child patient can also reduce medical costs by eliminating the need for anaesthesia during procedures, such as lumbar puncture or radiotherapy, minimizing the use of expensive pain medications, and decreasing the number of nurses required to complete painful procedures. Certified Child Life Specialist Morgan Livingstone (Toronto) has developed a series of practical on-the-job child-life

training courses for medical professionals and auxiliary staff, adapted for resource-limited settings, and including nonpharmacological pain management, effective procedure preparation, distraction play, and comfort positioning. Her program has demonstrated the value of simple measures to reduce a child's anxiety and increase co-operation during painful procedures, such as therapeutic massage to control pain. Nonverbal and distressed children can express their feelings and understanding of their medical experience through the use of simple cloth dolls, and medical staff can use these dolls to explain medical procedures in a nonthreatening way (Figure 2). Printed educational resources illustrating the process of eye removal and living with a special eye provide further emotional support and aid the dissolution of stigma, which currently impedes acceptance of therapy and postoperative psychological healing.

Further proposals involve the development of a national support network through which families can connect, share experiences, and become empowered through mutual support. In the long term, DECF will encourage construction and locally funded maintenance of a family hospitality house in Nairobi, to serve families whose children require intensive therapy to save sight or life.

Expected impact and outcomes

The KNRbS will directly benefit over 1000 individuals, including children with retinoblastoma, their families, medical professionals, and other personnel working in the retinoblastoma field over the 5 years of the program. Hundreds of primary-care workers will learn about childhood eye cancer and be better equipped to recognize and refer suspect cases promptly. An estimated 86 Kenyan children are newly affected by retinoblastoma annually, and a further 40-50 children with retinoblastoma travel to Kenya from neighbouring countries each year for medical care. Improved care could redress the significant negative effects of financial, practical and social burdens of childhood cancer on family life.

Dr. Dimaras is a postdoctoral fellow in the Global Retinoblastoma program at the Hospital for Sick Children, Toronto. Ms. White is the Founder and Executive Director of Daisy's Eye Cancer Fund. Dr. Gallie is the Medical Director of Daisy's Eye Cancer Fund, Head of the SickKids' Retinoblastoma Program, and Professor of Ophthalmology, University of Toronto.

Daisy's Eye Cancer Fund is dependent on voluntary donations from the public. The 2007 Blind Ball and generous donations in honour of Canadian musician Jeff Healey have specifically funded Rati's Challenge in Africa.

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