

# Challenges and opportunities to advance pediatric neuro-oncology care in the developing world

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## Abstract

**Purpose** As the morbidity and mortality associated with communicable diseases continue to decrease in the developing world, the medical burden of childhood cancer continues to expand. Although international aid and relief groups such as the World Health Organization recognize the importance of childhood cancer, their main emphasis is on the more easily treated malignancies, such as leukemias and lymphomas, and not pediatric brain tumors, which are the second most common malignancy in children and the leading cause of cancer-related deaths in the pediatric population. Addressing the needs of these children is a growing concern of several professional neuro-oncology-related societies. Thus, the goal of this review is to describe the current state of pediatric neuro-oncology care in the developing world, address the current and future needs of the field, and help guide professional societies' efforts to contribute in a more holistic and multidisciplinary manner.

**Methods** We reviewed the literature to compare the availability of neuro-oncology care in various regions of the developing world with that in higher income nations, to describe

examples of successful initiatives, and to present opportunities to improve care.

**Results** The current challenges, previous successes, and future opportunities to improve neuro-oncology care are presented. The multidisciplinary nature of neuro-oncology depends on large teams of highly specialized individuals, including neuro-oncologists, neurosurgeons, neurologists, radiologists, radiation oncologists, pathologists, palliative care specialists, oncology nurses, physical therapists, occupational therapists, speech therapists, pediatric intensivists, and social workers, among others.

**Conclusion** Pediatric neuro-oncology is one of the most complex types of medical care to deliver, as it relies on numerous specialists, subspecialists, support staff, and physical resources and infrastructure. However, with increasing collaboration and advancing technologies, developed nations can help substantially improve neuro-oncology care for children in developing nations.

**Keywords** Brain neoplasms · Developing countries · Health care disparities · Humans · Needs assessment · Socioeconomic factors

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## Introduction

Tumors of the central nervous system (CNS) are the most common solid neoplasm and leading cause of malignancy-related death in children. CNS malignancies represent approximately 16.6 % of all childhood malignancies, with a slightly higher incidence in male patients. Children with CNS malignancies do not have as favorable of a prognosis as those with non-CNS malignancies nor has their survival dramatically improved in recent decades, as has that of children with other types of cancer [1].

Given the relative frequency of CNS tumors, an increasing amount of comparative epidemiological data is available for pediatric CNS tumors outside of the Western world, though comprehensive and consistent data are still lacking. Notably, racial differences in the incidence of brain tumors have been noted [1–3], and socioeconomic comparisons have suggested that brain tumors tend to affect individuals in industrialized nations more frequently than those in developing nations. Whether this represents ascertainment bias due to differences in access to care, diagnostic capability, or health literacy remains unknown [4].

Nearly 86 % of the world's children live in developing countries [5], and 80 % to 90 % of the 250,000 new cases of pediatric cancer each year are diagnosed in a developing nation [5, 6]. Studies based in the USA have estimated that the cost of hospitalization, surgery, chemotherapy, radiation therapy, laboratory studies, and pharmacy services are 32,000 to 45,000 (US\$) for the first year after a brain tumor diagnosis. Subsequent annual costs are 4000 to 8000 (US\$) [7]. This represents an unrealistic burden in developing countries, where approximately 26 % of the population subsists on less than 1 (US\$) per day [8].

The prevalence of cancer in developing nations is increasing as child health improves and infectious diseases are better controlled [8, 9]. To further complicate matters, these nations have been largely excluded from the progress in pediatric cancer treatment; pediatric populations account for 4 % of all cancer-related deaths in low-income countries versus 0.5 % in high-income countries [8]. This review aims to analyze the status of pediatric neuro-oncology services in the developing world, with an emphasis on defining the current state of the field and identifying shortcomings and solutions to the problems at hand. The challenges and opportunities of key issues are presented, as are some examples of successful efforts.

## Creating cancer registries

### Challenges

The World Health Organization (WHO) has encouraged the development of cancer registries as a step toward preventing and controlling cancer in developing nations. Cancer registries are collections of data (i.e., age, sex, ethnicity, histology, working diagnosis, disease staging, and patient outcomes), ideally with data on every person diagnosed with cancer in a geographic population. These data are essential to establishing epidemiologic patterns of cancer that are endemic to particular regions or populations. Cancer registries provide invaluable information about disease burden, identify disease causes and changes in cancers, and help establish priorities for combating cancer in resource-poor areas [10–12].

Despite the known benefits of cancer registries and encouragement from the WHO and other organizations, most developing regions consider such efforts a luxury. Instead of investing in future needs, they focus their limited resources on providing care and support to current patients. Data from 2006 estimate that only 8 % of people in Asia, 11 % in Africa, and 21 % in Latin America are covered by cancer registries. Conversely, 99 % of people in the USA and Canada, 86 % in Australia and New Zealand, and 57 % in Europe and Russia are covered [13]. Overall, only about 20 % of the world's population is covered by cancer registries [14].

Other substantial challenges to establishing quality cancer registries in developing regions are inadequate health care infrastructure, inconsistent medical and legal record keeping, unstable populations and socioeconomic conditions, language and educational barriers, and cultural attitudes regarding medical care [10]. In one series, only 3 of 16 African cancer registries reported microscopically confirmed diagnosis in more than 70 % of their cases [11]. Similar issues have been seen in Asian and Latin American registries. Many developing nations do not require death certificates to be filled out by trained medical personnel, and many deaths go unreported [10, 11]. Therefore, it is impossible to calculate cancer mortality rates and survival times in those regions [11].

Another hindrance to establishing quality registry data, particularly for the pediatric population, in many developing nations is a possible gender bias in pediatric cancer diagnoses [10, 15]. A report based on the 1998 volume of the *International Incidence of Childhood Cancer* [16] demonstrated that the incidence of pediatric cancer in the nine lowest income countries has a male/female ratio that is greater than 1.5:1 [15]. Pakistan and Afghanistan have reported male/female incidence ratios of greater than 2:1 [17]. Although this disparity may reflect differences in the population, nonmalignancy-related childhood mortality, cancer incidence, or gender-based differences in disease progression, it most likely reflects the higher incidence of male children receiving a diagnosis and treatment [15]. Previously successfully implemented systems have attempted to minimize this problem by requiring that all patients with cancer who are referred to the hospital be included in the registry, regardless of treatment status, outcome, or treatment protocols used [10].

Establishing quality cancer registries requires a large effort, in terms of manpower and financial resources. Dedicated personnel must be assigned to input and maintain data continuously. Health care practitioners must be committed to following up on registry parameters to ensure that the data are complete and up to date. Information technologists must be made available to provide hardware and software support and development [18].

## Opportunities

Initial strategies for establishing cancer registries are focused around the existing medical infrastructures. In developing nations, most cancers, especially pediatric cancers, are treated in major academic referral centers. Therefore, establishing hospital-based registries at those centers is a first step toward establishing protocols and data. These registries would further benefit from their lower financial impact and greater internal consistency compared to population-based registries [10, 19]. Twinning programs with pediatric cancer centers in developed nations also could oversee new registry programs and establish collegial alliances between centers. However, larger population-based registries, beyond the initial footprint of referral centers, remain the gold standard for establishing comprehensive data [10].

## Examples of success

Uganda has successfully implemented the Kampala Cancer Registry, which is the oldest and largest population-based cancer registry in Africa. The registry uses the CANREG system, which is available free of charge [10], and has greatly helped to establish national disease burden, prioritize areas for prevention and treatment, and identify factors that influence disease course [20]. This registry is about 90 % complete [21] and serves as an example for other developing nations.

Another success story is the Pediatric Oncology Network Database (POND), which serves as a free, multilingual online database for pediatric oncology patients and caregivers in resource-poor areas. The goal of POND is to provide an electronic database in which to store and share patient data in a uniformed way and allow meaningful data collection and analysis across international and linguistic barriers. As of 2012, POND reported more than 1200 users from 233 sites in 66 countries, contributing to more than 50,000 patient records. This application has seen continued growth and success, especially at the Unidad Nacional de Oncología Pediátrica clinic in Guatemala, which accounts for nearly 50 % of the monthly logins and data shares and more than 70 % of the approximately 1000 reports generated each month. However, these advances are limited by technological availability, and the most successful programs have benefitted from dedicated funding from outside institutions [22].

## Implementing a multidisciplinary team approach

### Challenges

In general, pediatric oncology represents a substantial challenge for developing nations due to inadequate access to pediatric hematologists and oncologists, a shortage of trained

experts in pediatric cancer histology and imaging, a lack of dedicated pediatric cancer units, and inadequate diagnostic testing and imaging capabilities. Some nations do not have a single trained pediatric oncologist or a dedicated pediatric cancer unit [23].

The data on pediatric neuro-oncology capabilities in developing nations is even more limited than that of pediatric oncology, though it is safe to assume that there are even fewer facilities capable of delivering adequate neuro-oncologic care, given the increased personnel and infrastructure requirements. The interdisciplinary nature of neuro-oncology requires extensive input from numerous specialists to establish the correct diagnosis, deliver appropriate and effective treatments, and maximize patient outcomes. Neuro-oncology, in particular, depends on large teams of highly specialized individuals, including neuro-oncologists, neurosurgeons, neurologists, radiologists, radiation oncologists, pathologists, palliative care specialists, oncology nurses, physical therapists, occupational therapists, speech therapists, pediatric intensivists, and social workers, among others. Optimal delivery of this type of care depends on communication and interaction among individuals who have a wide variety of expertise, each with knowledge of the specific benefits and risks of various forms of care to be provided. Frequent and clear communication is especially important, considering the commonality of complications and recurrence of disease [24].

## Opportunities

A 2011 web-based survey that assessed the availability of resources for treating pediatric brain tumors in the developing world demonstrated a positive correlation between the number of patients treated and the availability of a dedicated neuro-oncology team. This finding suggests that centralizing pediatric neuro-oncologic services will help establish the appropriately specialized care teams required to take care of these patients by concentrating resources and establishing adequate patient load to make these care teams a viable reality. However, centralization also may further deprive those patients who are unable to reach the centers due to geographic, infrastructural, or transportation challenges. Thus, issues such as providing adequate transportation, housing, and accommodations to patients and caregivers are essential to ensure the viability of this solution [25].

## Establishing clinical pediatric neuro-oncology programs in developing countries

### Challenges

In the 1960s–1970s, new technologies in the fields of radiologic imaging, oncology treatment, chemotherapy, and

pathologic assessments, along with the continued advancement of neurosurgical procedures allowed greater multidisciplinary medical management of brain tumors [26, 27]. As of 1999, neuro-oncology societies across the world reported having approximately 1000 members [26]. However, given the broad, multidisciplinary nature of caregivers and the variety of training backgrounds of neuro-oncologists, neuro-oncology is not a board-approved subspecialty, even in the USA [26]. Therefore, calculating the actual number and distribution of formally trained neuro-oncologists worldwide is a difficult challenge.

### Opportunities

A crucial first step toward establishing neuro-oncology programs in developing nations is to define the need. There are minimal data on the state of pediatric neuro-oncologic care in developing countries, with most of the existing data consisting of single case reports and small series. Studies should be undertaken to quantify the current standards of care and identify shortages in personnel, equipment, and medications [28]. Once a baseline is properly established, specific goals and interventions can be meaningfully set.

Despite the paucity of information, some previous attempts to identify and remedy this problem have been reported. In a 2008 speech to The Society for Neuro-Oncology (<http://www.soc-neuro-onc.org>), the International Brain Tumor Alliance Secretary Kathy Oliver called for improved access to basic medications to palliate symptoms in areas where access to modernized neuro-oncologic care is not possible [28]. The same year, neuro-oncology specialists at Groote Schuur and the Red Cross Children's hospitals (Cape Town, South Africa) instituted a brain tumor workshop coinciding with a meeting of the International Society of Pediatric Neurosurgeons (<http://www.ispneurosurgery.org>). From the concurrent ISPN conference, organizers of the workshop recruited experts in the field to deliver keynote addresses, case presentations, and lectures. This workshop has become an annual event that draws attention to brain tumors on the African continent [27].

### Examples of success

One of the most effective and immediate steps that can be taken is collaboration between developed and developing nations. "Twinning" refers to the collaboration and sharing of expertise and resources between institutions in developed and developing countries [6]. This model has effectively improved the outcomes of various diseases, including pediatric medulloblastoma. A 12-year-long partnership between specialists at King Hussein Cancer Center (Amman, Jordan) and those at the Hospital for Sick Children (Toronto, Ontario, Canada), consisting of regular e-mail interactions, exchange visits at

both institutions, and videoconferences, has resulted in Jordanian survival outcomes approaching that of westernized nations [29]. Similarly, in Paraguay, treatment guidelines for common pediatric brain tumors have been developed based on available resources in order to standardize care and improve patient outcomes [30], and the International Society of Paediatric Oncology (SIOP; <http://www.siop-online.org>) recently published guidelines for treating medulloblastoma that are specifically for resource-limited areas [31]. Furthermore, organizations such as SIOP, the Society for Neuro-Oncology, and the International Symposium on Pediatric Neuro-Oncology (<http://www.soc-neuro-onc.org/events/105/>) offer opportunities such as travel scholarships (to work in resource-poor areas and translate resources and treatment guidelines), conferences, and other professional outreach events in developing areas that provide direct engagement.

Most of the literature describing the field of neuro-oncology as a whole is based on information gathered in western nations. Because neuro-oncology is so multidisciplinary, the issues central to developing it as a specialty encompass multiple specialties (i.e., pediatric neurosurgery, radiation oncology, neuropathology, neuroradiology, palliative care, and ancillary services) [26]. These specialty-specific issues are detailed in the following sections.

### Pediatric neurosurgery

#### Challenges

Neurosurgical intervention is an essential component of neuro-oncology care. Although CNS tumors can rarely be treated with surgery alone, the patient's outcome often depends on the degree of surgical debulking, and in some cases, cure is possible through resection alone [24]. Furthermore, the role of the surgeon is one that cannot be realistically handled in a long-distance manner, whereas clinical, radiologic, and pathologic information has the potential for effective long-distance consultation via advanced telemedicine and electronic communication [32].

Africa, which is home to approximately one billion people, has about 1200 neurosurgeons. Of these, only 142 are located in sub-Saharan Africa (excluding South Africa), which translates into one neurosurgeon per five million people [33]. Similar trends are seen in other developing regions. The WHO estimates that Southeast Asia has approximately one neurosurgeon per three million people, and Eastern Europe and the Western Pacific have approximately 1 neurosurgeon per 250,000 [34]. More favorable ratios are seen in Europe (1:121,000) and North America (1:81,000); the ratio of neurosurgeons to the world population is 1:230,000 [35]. Geographic disparities are also seen within countries. For instance, 12 of the 15 neurosurgeons in Kenya are located in the city of

Nairobi [33]. As of 2001, numerous African nations, including Niger, Mali, Mauritania, Equatorial Guinea, Guinea Bissau, Lesotho, Swaziland, Rwanda, Madagascar, Comoro Islands, and Burundi, which encompass a total population of more than 46 million people, did not have a single neurosurgeon [35].

Geographic disparities also exist in terms of neurosurgical equipment. In 2001, the WHO Working Group in Neurosurgery published data from 44 African countries. Only northern nations and South Africa had adequate CT scanning equipment, and within those countries, much of the population's access is limited due to socioeconomic factors. They also reported a lack of surgical equipment in 37 nations and shunts in 14 nations [36].

The optimal ratio of pediatric neurosurgeons to population is about 1:150,000 to 1:400,000. Detailed information about the state of pediatric neurosurgery in the developing world is limited. Nonetheless, in 2007, the number of pediatric neurosurgeons in select countries throughout the world was estimated. Nine of 10 of the surveyed countries that failed to meet the minimal recommended ratio of pediatric neurosurgeons were in developing regions [37]. As of 2012, there were no more than 12 pediatric neurosurgeons in all of Africa. This is especially a concern because approximately 50 % of the population of most African countries is younger than 18 years. Therefore, the need for pediatric-trained specialists is especially great [33]. Needless to say, the number of neurosurgeons, let alone pediatric-trained neurosurgeons, in Africa falls well short of the optimal ratios [38].

The underdevelopment of neurosurgical resources in Africa is related to the financial and social instability that plague all areas of medical care. However, the super-specialized nature of the discipline further hinders its development. Low-income nations frequently divert resources to community health and primary care specialties because those services treat a greater number of people than would a neurosurgical service. However, the need for tertiary care specialists will continue to be great, regardless of the state of primary care fields. As such, it has been proposed that these fields be developed in tandem, rather than in a serial manner [38].

## Opportunities

Previous efforts have focused on transporting patients to neurosurgical facilities in developed countries or bringing trained neurosurgeons to areas of need. However, this is not a sustainable solution. Local patterns of disease, including tumor types, infection risks, and cultural influences, are unique to those areas. Thus, locally trained and practicing neurosurgeons are essential for providing optimal care [32]. Other strategies have included neurosurgeons from developing countries receiving training in developed countries and then returning home to practice.

However, this approach can lead to incomplete training, maladaptation to practicing upon the surgeon's return, and delayed implementation of neurosurgical services while surgeons are training abroad [36, 39]. In Africa, local neurosurgical training is available in relatively wealthier developing countries, though the programs are plagued by outdated information, isolation, and limited access to neurosurgical resources, societies, and meetings [36]. Traditional medical mission trips are not beneficial to neuro-oncologic conditions because surgical treatment of CNS tumors does not lend itself to large-volume, scheduled operations, as do other conditions such as cleft palate or cataracts. Most importantly, neither of the solutions addresses the root problem in a sustainable manner. Consequently, outreach missions must be geared toward teaching local providers surgical techniques in order to create a sustainable model of care.

Other proposed solutions to the neurosurgeon deficit include establishing pediatric neurosurgical programs at existing hospitals, increasing access to educational resources through neurosurgical societies, extended visits from neurosurgeons, establishing donation relationships between developed and developing countries, and training general surgeons to perform basic neurosurgical tasks [33, 36, 37]. A 2005 report on neurosurgery in Africa encouraged neurosurgeons to claim some level of responsibility for this disparity. Although the report acknowledged that the resources, equipment, and patient outcomes may be suboptimal, it encouraged African neurosurgeons to keep a positive attitude and among health care planners and the general public defend the need to develop neurosurgical services [39].

## Examples of success

The outreach mission approach has shown short-term promise in Peru. Local surgeons were trained in selected neurosurgical techniques over the course of 3 years. They were then allowed to independently perform 196 surgeries during the following 5 years [33, 37]. Another example of success is the Foundation for International Education in Neurological Surgery (<http://www.fiens.org/>), which has sent volunteer neurosurgeons to more than 22 developing countries to train local surgeons in procedures and establish sustainable residency programs. Similarly, the World Federation of Neurosurgical Societies (<http://www.wfns.org/>) works with 124 neurosurgical societies across the globe to provide education and equipment to areas in need. The African branch of this organization, the Pan African Association of Neurological Sciences, publishes a biannual journal, the *African Journal of Neurological Sciences* [36]. Training non-neurologic surgeons in neurosurgical procedures may provide some relief while long-term solutions are being studied and implemented [34].

## Radiation oncology

### Challenges

Radiation oncology is central to the care of patients with CNS malignancies. Australian registry data estimated that 92 % of patients with a CNS malignancy met indications for radiotherapy at least once during their disease course [40]. This represents the highest proportion of all cancers analyzed and far exceeds the average optimal radiotherapy utilization rate of 52 % for all cancers [40, 41]. Furthermore, radiation is often the best palliative measure available, especially for patients presenting with advanced-stage disease, as is often the case in developing nations [41–46]. However, the challenge of establishing radiation oncology services in developing nations is substantial and complex, requiring considerable immediate and long-term investments and commitment [41–47].

Recent cost estimates for constructing the physical infrastructure required for radiation oncology range from 40,000 to 1,000,000 (US\$), and the megavoltage radiation machines used to deliver external beam radiation therapy range from 480,000 to 1,800,000 (US\$), not including maintenance costs [41]. Depending on the country and machine type, the cost of a single facility can easily exceed tens of millions (US\$) [45]. Additional costs not accounted for in these figures include simulation and planning computers, software and hardware updates, replacement radioactive materials, and wages for physicians, medical physicists, technologists, and engineers [41, 45].

There is a socioeconomic disparity among nations, in terms of their access to radiation oncology facilities. A nation's gross national income per capita has a strong positive correlation with its number of radiotherapy machines per million people, and wealthier nations possess a disproportionate number of machines [41, 43–45, 47]. Among developing nations, radiotherapy resources are found predominantly in populous nations. Countries with at least one radiotherapy machine have a mean population almost 12 times that of nations without any services [47]. Recent studies estimate that 29 countries in Africa and 13 in Asia completely lack radiotherapy capabilities [41, 46].

Africa has the worst discrepancy between need and availability of radiotherapy resources: Almost 21 % of the population has no access to radiotherapy. The total supply of megavoltage machines meets only 18 % of the anticipated need, and the machines are distributed with great regional disparity. Southern Africa has as many as one machine per 3.4 million people, but the western region has as few as one machine per 24 million [41]. Sixty percent of the radiotherapy machines in Africa are located in Egypt and South Africa. In areas of North America, the distribution is no less than 1 per 70,000 [46].

Substantial disparities between supply and demand, though less pronounced, also exist in other developing regions of the world. An analysis of 17 low- to middle-income Asian/Pacific nations revealed a deficit of nearly 5000 machines, though the real need is probably far greater [41]. India's deficit was more than 700 machines in 2006, despite having a publically funded national cancer control program for nearly four decades [42]. Mongolia and Thailand were the only nations that had, on average, at least one treatment-planning station per department, and only Mongolia and Singapore had, on average, at least one simulator per radiation oncology department [41, 43].

A survey of 19 low- to middle-income Latin American countries revealed less disparity than their African and Asian counterparts, though 75 % of the machines were located within the four most populous countries [44]. Only 19 % of the radiotherapy centers in Latin America had simulators; only 45 % had equipment necessary for calculating proper dosages, and most nations had no more than one trained radiation oncologist. [41, 44] Despite these deficits, 12 of the countries have locally based training programs for radiation oncologists, and 7 have training programs for medical physicists. However, only 60 % of the need for radiation oncologists is met, and less than 50 % of the need for medical physicists and radiotherapy technologists is met [44].

All Eastern European countries offer some level of radiotherapy service. However, analysis of data from the region's 22 low- to middle-income nations revealed that only Slovakia meets more than 50 % of the predicted demand [41]. Despite the relative abundance of radiotherapy resources in the region, the radiotherapy technology that exists in many Eastern European nations is outdated or obsolete and in need of replacement in addition to expansion [41, 45].

### Opportunities

Despite the large investment and overhead required to provide radiotherapy services, the long service life of equipment and infrastructure combined with the high volume of patients who can be treated on an outpatient basis with a single machine makes radiation oncology a highly cost-effective treatment method [41]. Previous studies have shown that radiotherapy can be more cost-effective than corresponding analgesic and chemotherapeutic drug regimens [48], thus providing additional incentive for the development of these services in resource-poor areas.

Closing the gap between supply and need will be challenging, and solutions should be tailored to each nation. Some believe that nations without radiotherapy capabilities should build at least one center, thereby offering treatment options to populations acutely in need [41]. Others emphasize that further developing existing facilities to their greatest potential will ensure that quality care is delivered prior to expanding

services [44]. Perhaps the most important goal is to develop sustainable, high-quality, and adequate training programs for physicians and support staff to create a system that is ultimately tailored to the medical and cultural nuances of each locality [41, 44].

## Neuropathology

### Challenges

The field of pathology faces challenges similar to those of other medical specialties in developing countries, with many countries hosting only a few, if any, pathologists [49]. Pathology and neuropathology represent a skill set that is not only reliant on individual proficiency in a variety of procedural and diagnostic tasks but also costly in terms of tissue stains and equipment [49, 50]. The specialized nature of the field generally limits its practice to large academic centers that depend on government funding, which is often unreliable in developing nations [50]. Furthermore, there is little consensus internationally regarding what training and certification qualifies one as a neuropathologist. [51] Unsurprisingly, there is little data on the status of neuropathology in the developing world.

India, Poland, Brazil, and Russia have formal neuropathology training programs, but these nations are relatively wealthy compared to most nations in the developing world [51]. In terms of general histopathology, Pakistan has only three or four hospitals with adequate services for their entire population of 160 million [52]. Uganda has 0.64 pathologists per million citizens, and Tanzania has 0.39 pathologists per million [49]. Others have estimated that an ideal ratio of neuropathologists to population is 1.5 neuropathologists per million [51].

Although no comprehensive data detailing the global distribution of neuropathology (let alone pediatric neuropathology) are available, one can predict that there is a wide geographic disparity and an overall shortage. A 1991 editorial in the *Journal of Brain Pathology*, the official publication of the International Society of Neuropathology, reported that the continents of Africa and South America accounted for only nine subscriptions to the journal; 95 % of the total subscriptions were from North America, Western Europe, and Japan [53]. Although this does not represent a comprehensive census of neuropathology services worldwide, it suggests a widespread shortage.

Unique issues are hindering the growth of this field in developing regions. First, as with other specialized neurologic services discussed, neuropathology training and professional organizations are found only in wealthier nations. Second, the definition of what constitutes a *neuropathologist* varies. Different regions require different levels of training, ranging from basic science only to requiring medical degrees and

fellowships, and there is little coordination among professional societies in nations where they exist. [51] Third, the donated equipment from more developed regions is often outdated and prone to malfunction. Because maintaining such equipment requires specialized training and equipment, those machines tend to remain broken. Staining reagents also can be costly and difficult to acquire and store properly [49]. Finally, neuropathology largely depends on the status of neurosurgical services; it is nonsensical to have neuropathology in areas where no one is capable of obtaining tissue specimens [51]. This is especially true for neuro-oncology, where histopathologic analysis is central to proper diagnosis and treatment, with consequences for patient care and accurate epidemiologic study [49, 51, 54].

Providing optimal care for pediatric patients with CNS malignancies is further compounded by the need for trained pediatric clinicians and surgeons, as well as pathologists familiar with the specifics of pediatric disease. There is only one hospital on the entire continent of Africa that is capable of delivering fully integrated pediatric pathology services, and that facility is located in the relatively wealthy nation of South Africa [54]. The status of pediatric neuropathology at that hospital, however, is unknown.

### Opportunities

Developing neuropathology services has some unique limitations, but established pathology services in developing nations can provide direction. Internet- and telemedicine-based review and oversight represents one of the most promising avenues to develop pathology specific to pediatric neuro-oncology because it enables pediatric neuropathologists to be involved, rather than relying on untrained or undertrained pathologists [50]. This approach can further facilitate long-distance consultation with pediatric specialists and provide educational opportunities [54].

Local, sustainable services should aim to minimize the role of specialized technology and emphasize obtaining supplies. One example of this is the “squash” preparation, a method that can be used in pathologic analysis of intraoperative samples that does not require freezing and sectioning [50]. In the absence of specialized immunostains and equipment, training programs must emphasize visual characterization of tissue and cellular morphology with minimal resources [50, 54].

### Examples of success

One such collaboration between the Instituto Materno Infantil de Pernambuco (Recife, Brazil) and St. Jude Children’s Research Hospital (Memphis, TN) showed that static (transmission of single, static images) and dynamic (real-time, continually transmitted images) telepathology are equally effective in establishing proper histologic diagnosis. This is

particularly beneficial, as the static method is less expensive and requires no real-time collaboration between professionals [55].

Similar strategies have been attempted with ground- and air-shipping services. Deetz et al. analyzed hematopathologic specimens from 582 cases over a 13-year period in collaboration between Washington University (St. Louis, MO) and facilities in the nation of Eritrea. This method has the advantage of using existing infrastructure without relying on modern digital technology, though it is limited by relatively slow turnaround time and follow-up. Furthermore, although 92 % of the samples in this study were in adequate condition for analysis, no corresponding data exists for CNS tissue samples [56].

## Neuroradiology

### Challenges

Neuroimaging plays a central role in the diagnosis and characterization of tumors. It is an integral component in planning and monitoring proper treatments and responses, in assessing a patient's surgical candidacy, and in identifying early treatment failures [57]. Inadequate imaging can lead to outright failure to diagnose or an inability to optimally manage disease course, thereby contributing to increased disease burden [58]. Imaging is especially important in CNS tumors because biopsy and histologic confirmation may not be possible due to the location of the tumor [59, 60].

The unavailability of neuroimaging, mainly resulting from limited physical resources and exorbitant costs of imaging studies, is a main obstacle to proper diagnosis and treatment of CNS tumors in developing nations. It is not surprising that these nations report a drastic need for modern imaging technology. Analysis of data from the WHO's 2010 international survey of medical devices showed that high-income nations have 142 times the MRI capability of low-income nations, 53 times the CT capability, and 555 times the PET capability, as adjusted for population [61]. Most African nations have less than one CT per million citizens. Twenty-two low- or middle-income nations reported having no MRI machines, and seven reported having no CT machines [58]. Additionally, only a few radiologists are working in developing nations, and even fewer are practicing in the public sector [62].

Pediatric neuroradiology was borne out of the recognition that the developing CNS undergoes drastic changes that can be seen on radiographic images [63]. No literature has specifically addressed the status of pediatric neuroradiology in the developing world; however, based on the inadequacy of radiographic equipment and personnel, we assume that pediatric neuroradiology resources are insufficient to meet the needs of those regions.

### Opportunities

Much like the development of radiation oncology and pathology services, that of neuroradiology programs requires an initial investment in infrastructure, equipment, maintenance, skilled radiologists, nurses, and technologists and a consistent, affordable supply of contrast agents [58, 64]. Governmental and nongovernmental partnerships between developed and developing nations have been implemented that allow physical resources and expertise to be shared across socioeconomic borders. Some steps that have been taken include providing mobile imaging technology to improve access to rural regions and wirelessly transmitting images from remote locations to radiologists regionally or abroad. Technologists' skills, the transmission of complex images, inadequate numbers of technologists and radiologists, and the lack of sustainability make these solutions suboptimal [58].

The availability of USA-based radiology training programs with international opportunities remains low compared to that of other specialties. Nonetheless, local radiologic education of medical and paramedical staff has been initiated in countries such as Haiti and India, where hands-on training is combined with online didactic materials. As technology continues to develop at rates that outpace that of infrastructure, the need to integrate radiographic technologies with wireless and mobile computing capability becomes increasingly important [58]. However, developing self-sustaining, locally based training programs is essential, as the technology, skills, and disease presentation encountered in training programs may not translate across socioeconomic or geographic borders [62].

## Palliative care

### Challenges

The WHO defines palliative care as “the active total care of the child's body, mind, and spirit and it involves giving support to the family” [65]. This philosophy of care emphasizes quality, dignity, and comfort for the patient and family, regardless of the patient's prognosis or pursuit of a curative intervention. It is also intended to aid in the bereavement and advanced-planning process, should it become necessary. Although the role, scope, and availability of palliative care teams continue to evolve, pediatric palliative care (PPC) teams ideally include specially trained physicians, care coordinators, bereavement specialists, child psychologists, and child-life specialists [66].

A 2011 study based in Lebanon that assessed the state of PPC at a single pediatric cancer center showed that almost all children experienced significant suffering from at least one symptom, and more than half suffered from five or more symptoms. PPC teams work with not only a population in



various stages of development whose needs are drastically different from those of the adult population but also their parents. Therefore, PPC teams should ideally extend from the hospital to the patient's home and school [65].

Barriers to PPC in developing nations include a lack of a defined legal/medical role, conflicts in decision making about treatment options, inadequate financial resources, and a lack of trained professionals. Parents further identified problems with regards to PPC, including increasing accessibility to home medical equipment, involvement in end-of-life health care decisions, and the financial impact of taking care of their child. Specifically, in nearly half of cases, parents reported financial difficulty often related to reduced work hours or quitting work altogether [65]. This study is consistent with those from the USA, which have shown that most caretakers of children with brain tumors had to reduce work hours; 16 % reported that they had to quit their job. Half of all households with a patient undergoing treatment for a brain tumor reported a decrease in household income that resulted in a threefold increase in the number of households living at or below poverty levels [67]. These hardships will most likely have a greater effect on patients in developing nations, given the scarcity of financial resources and social support, as well as the greater role of young people in the workforce [5].

Almost one third of patients' parents reported that they were unprepared for health-related issues that arose during the final month of their child's life. Other challenges to parental adjustment to end-of-life care included fear about their child's condition and a sense of parental failure [65]. Although the origin of these issues is multifactorial, two thirds of parents who reported feeling unprepared felt that they were not involved in their child's advanced care planning [68]. This is consistent with preconceived notions that historically conservative cultures prefer to not discuss end-of-life topics [69]. However, studies from Jordan, a predominantly Muslim nation, showed that parents of children with brainstem glioma prefer early and honest disclosure about their child's prognosis and resuscitation status, despite cultural preconceptions to the contrary [60, 69], and most parents accepted the concept of palliative treatment [60].

### Opportunities

Parents from the Lebanese study identified the positive aspects of PPC, including spiritual and prayer-based support. They also emphasized the importance of family and social ties [65]. Together, these studies demonstrate that the optimal PPC model in developing nations addresses the same needs as western models [69]. This includes a multidisciplinary approach with medical and nonmedical teams [68], initiated early during treatment regardless of treatment goals [68], with upfront and honest communication with caregivers and

families [60, 66, 69]. However, the challenge of instituting PPC programs in resource-limited nations remains great.

### Ancillary services

#### Challenges

Comprehensive care of the pediatric patient with CNS malignancy depends on the involvement of ancillary services (i.e., speech therapy, audiology, physical therapy, occupational therapy, anesthesiologists, and pediatric intensivists). These services are frequently lacking, in terms of staffing, financial capability, and equipment resources, in developing nations. In a 2008 survey of 62 countries, 86 % of respondents indicated a need for more audiologists and a lack of standardized training [70]. Little comprehensive data exist on the adequacy of physical therapy and speech therapy services internationally.

The challenges faced by ancillary services parallel those of the other medical resources described here. A 1992 analysis of developing occupational therapy services in resource-poor nations emphasized the need to develop services that are in line with a particular area's causes of morbidity and mortality, to make the services accessible to areas in need outside of population centers, and to ensure that the services are sustainable [71].

#### Opportunities

Although written with occupation therapy in mind, the steps toward remedying these deficiencies can be applied broadly to other support services. In addition to understanding the extent and types of disability encountered, we must create a patient-centered model within the existing cultural norms and health care infrastructure, rather than focusing on westernized practice paradigms. Also, we must demonstrate the benefit of these services to establish local educational opportunities to provide sustainable, culturally sensitive models of education [71].

### Conclusion

Pediatric neuro-oncologic care in the developing world needs to be substantially improved. Much of the world lacks the basic expertise and/or equipment needed to diagnose and treat children with brain tumors and to support their families. As widespread poverty and political instability continue to threaten the delivery of health care to much of the world, it is no surprise that establishing pediatric neuro-oncology services remains a distant goal. Remedying this problem will require substantial collaboration between developed and developing nations. Hopefully, we will continue to gain ground, as advancing technology helps bring health care providers together.

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