Pediatric Leukemia, Psychosocial Dimensions of Cures, and Implications for HIV

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Although many aspects of HIV cure research in pediatric populations are entirely without precedent, historical examples demonstrate how curative interventions may transform clinical practice and perceptions of disease over time. The history of pediatric acute lymphoblastic leukemia (ALL) illustrates how the psychological and social dimensions of care became part and parcel of curative efforts. In particular, the tripartite concept of cure devised by physician and bioethicist Jan van Eys provides a framework for approaching curative research and clinical care in a pediatric population. As we slowly move toward an HIV cure, lessons learned from ALL and van Eys's work may help us implement such a cure more effectively in a pediatric context.

CHILDHOOD LEUKEMIA AND A TRIPARTITE CONCEPT OF CURE

Pediatric ALL underwent a transformation from incurable to curable in the second half of the 20th century. Before the 1950s, it was a uniformly fatal disease. Treatments such as blood transfusions could briefly prolong life, but clinical management focused on controlling symptoms and helping patients and their families prepare for death.¹ Beginning in the late 1940s, however, new chemotherapies

dramatically increased survival rates and, by 1980, ~50% of patients could expect to survive ≥ 5 years, creating a real possibility of future life for increasing numbers of patients.^{2,3} As survival rates increased, pediatric ALL was gradually reclassified from an incurable illness to one with a significant chance of remission and, eventually, cure.^{4,5}

In the mid-1970s, a crucial therapeutic transition period, pediatrician and bioethicist Jan van Eys noted that the ambiguous situation in which survival was possible, but not guaranteed, meant that patients and their caregivers (usually family members) often experienced years of uncertainty and anxiety. He wondered whether, if patients survived ALL but had lasting psychological or social difficulties, they were truly cured of the disease. In response, van Eys devised a tripartite concept of cure: a biological cure, which consisted of eliminating the disease from the body; a psychological cure, which resulted in feeling at ease with having or having had the disease; and a social cure, which involved the ability to participate in society as fully as possible. His ultimate goal was a "truly cured child," one who was not only physically well but also mentally healthy and

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functioning at an appropriate societal level.⁶

Although this emphasis on quality of life was not unique to van Eys,⁷ he was instrumental in providing clear and explicit reasons to promote and support the concept, particularly in the context of pediatric cancer.⁸ Just as importantly, he and his colleagues at MD Anderson Hospital & Tumor Institute (now the MD Anderson Cancer Center) worked to implement this vision of “truly cured” children, designing more welcoming pediatric oncology wards, advocating for multidisciplinary team approaches to care, and partnering with local schools to ensure that children could keep up with their studies. In addition, they held a series of conferences, aimed at different professional groups, focused on mental health in pediatric oncology.^{9–12}

This case shows how holistic psychosocial care can be integrated with improved treatment protocols to achieve contemporary cure rates of 80% for patients with ALL in modern medical centers.¹³ At the same time, this accomplishment has thrown into sharp relief the facts that adequate oncological resources are unavailable for most of the world’s pediatric population, that curative treatment in ALL poses a risk of long-term sequelae for survivors, and that caregivers of these patients experience psychological and socioeconomic burdens despite the high probability of cure for their loved ones.¹⁴ The successful experiences and persistent challenges treating pediatric ALL can inform ongoing efforts in HIV cure research.

HIV AND THE TRULY CURED CHILD

Recent developments indicate that HIV may make a transition similar to that of pediatric ALL, from an incurable to a curable disease.

Currently, HIV-infected people who adhere to prescribed antiretroviral drugs can achieve and maintain viral suppression for years; their prognoses are undoubtedly better than those of patients with ALL before the 1980s. However, antiretrovirals do not restore a person’s normal immune status and are associated with cardiovascular disease, bone disorders, and cognitive impairment. Long-term use increases the risk of these comorbidities and the likelihood of treatment interruption, which almost always leads to the reemergence of detectable viral loads and, in time, full-blown AIDS.¹⁵

The importance of psychosocial care is already recognized for pediatric patients with HIV. Treatment adherence, coping with daily life demands, and the identification of risks such as substance abuse are therefore important goals. Despite cultural variations in notions of health, disease, and treatment, a consensus is forming about the importance of training more specialized health workers, the need for collaboration with institutions beyond the clinic, and the pivotal role of disclosure management as a means to foster trust.^{16–18}

Implementing these recommendations is not always straightforward. Despite the reduction in rates of vertical HIV transmission in the United States, HIV prevalence among older children and teenagers in regions such as southern Africa will remain a substantial problem in the medium term.¹⁹ In these areas, long-standing poverty and a lack of therapies hampers the provision of psychosocial care. These pediatric patients with HIV face distinct difficulties, including the relative weakness of their social networks and the stigma attached to HIV.

Making room for psychosocial provisions in these lower-resource settings is difficult yet especially necessary.

A cure would change this landscape, and challenges may emerge from many angles. During the research phase, patients may misunderstand the uncertain outcomes of a given therapy and may suffer anxiety while waiting to determine whether treatment is successful. As we have learned from pediatric ALL, the emotional and social toll on caregivers may be significant and should be proactively addressed. In addition, patients who are improving may lose access to social or medical services if they no longer qualify as chronically ill. After treatment, stigmatization may persist even after the disease has been biologically cleared. Moreover, long-term sequelae may haunt pediatric HIV survivors, as they have pediatric ALL ones, necessitating ongoing surveillance.

The example of pediatric ALL also highlights the complexity of treating patients over periods of time. Although physicians may eventually agree on landmarks defining a cure for HIV, we will not know for years whether a treatment has been successful. As with ALL, throughout this process pediatricians will come to know patients in different phases of care: under treatment, in remission, and possibly cured. Moreover, health workers could be caring for patients through different development stages, which calls for a flexible approach to the delivery of psychosocial care. Oncology workers’ skills will be relevant because they are not naive about the challenges of growing with their young patients.²⁰ Likewise, as the ALL case shows, these workers have experience advocating for innovation in response to patients’ suffering, creating alliances between

medical and paramedical colleagues, anchoring care provision beyond hospital wards, and encouraging children and their caregivers to think of a future beyond patienthood. In the context of HIV in children and adolescents, a focus on promoting “truly cured” children will result in a population who not only have

survived HIV but who can thrive in its wake.

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ABBREVIATION

ALL: acute lymphoblastic leukemia

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