WHAT'S NEXT IN ENDING PEDIATRIC AIDS?

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FORWARD BY
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Elizabeth Glaser’s 7 year old daughter, Ariel, lost her battle with AIDS in 1988. It was because of her loss, and her fear for her son’s life, that Elizabeth visited Capitol Hill to insist on more funding for research on pediatric HIV. Elizabeth’s tenacity and unyielding will to save her son resulted in the creation of the Elizabeth Glaser Pediatric AIDS Foundation. In the spirit of Elizabeth Glaser, the Foundation has worked tirelessly to reach children infected and affected by HIV through advocacy, research and programmatic efforts over the last 25 years.

At the beginning of the AIDS epidemic in the United States, the Foundation would convene researchers for think tank style discussions to confront and debate the scientific challenges related to pediatric HIV, and were an early step in understanding the need to prioritize the unique requirements and barriers faced by children with HIV. In recognition of Elizabeth’s legacy and the Foundation’s 25th anniversary, the Foundation hosted a new type of roundtable on pediatric HIV in June of 2014. A modern take on the former think tanks, this event aimed to address not only the scientific issues facing pediatric HIV but the social and financial aspects as well. The roundtable brought together leaders in the HIV field, from world renowned scientists and researchers to representatives from implementing organizations, funders and government bodies. Robust panel discussions acknowledged Elizabeth’s legacy, reviewed the progress and the pitfalls that the field of pediatric HIV/AIDS faces today, and the steps to be taken to end AIDS in children once and for all.

With so many leaders in the field of pediatric HIV/AIDS together in one room, one expects a lively, engaged discussion. What was striking, however, was how committed the panelists were to taking real action. For example, the two premier US agencies working on pediatric HIV today not only talked about how their individual efforts would have greater impact on pediatric HIV outcomes and on child survival if government agencies worked together – they committed to aligning U.S.-funded child health and HIV/AIDS efforts to more effectively ensure that HIV-exposed and HIV-infected children survive and thrive. As UNAIDS, PEPFAR, and others have noted, we are at a critical tipping point in the HIV/AIDS pandemic; significant progress has been made since the beginning of AIDS, but increased efforts and collaboration like the ones discussed at this event are essential if we are to reach the end of pediatric AIDS.

We must leverage this progress to finish the job. The global response to HIV must move forward with the same strength Elizabeth Glaser demonstrated when trying to save her son – if not, the disease will once again outpace the response. It is time for the global community to double down on its efforts, to take bold, sustained, and strategic action, and commit to a future where no child has AIDS.
INTRODUCTION

On June 25, 2014, the Foundation hosted a high-level policy roundtable in Washington, D.C. as part of the Foundation’s 25th anniversary. This roundtable event brought together leaders in HIV/AIDS policy, implementation, and research to discuss the next generation of HIV science, the hunt for a cure, and new and emerging issues confronting the pediatric HIV/AIDS field.

While progress has been made in the fight against AIDS, significant work is still needed in order to address children infected and affected by the pandemic and to truly reach an AIDS free generation. Since 2001 new infections in children have declined by approximately 58%. However, nearly 240,000 children (0-14yrs) were still infected with HIV in 2013 and only 24% of HIV-infected children were receiving antiretroviral therapy. A business as usual approach will not help to reach the children slipping through the existing systems – additional efforts are needed in order to reach those children who are HIV-positive or at risk of HIV infection.

For these reasons the Foundation brought together leaders in the HIV/AIDS field for a thought-provoking discussion to illuminate the challenges facing pediatric HIV and to identify priorities needed to address this pandemic. The Foundation posed two questions to the panelists – (1) Where should investment in pediatric AIDS be concentrated? and (2) Where is the next game changing innovation for pediatric AIDS? The ensuing discussion highlighted progress in eliminating new pediatric HIV infections, new thinking on how to improve pediatric HIV treatment and retention, unique opportunities for developing new pediatric medicines and potentially a cure, and what all of this means for children impacted by the pandemic moving forward. The discussion was positive and maintained a sense of hope for what future investment could mean for children impacted by this challenging disease.

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Michael Gerson, Opinion Columnist for The Washington Post and a Policy Fellow with the ONE Campaign, moderated the panel discussion and opened by asking the panelists where investment is needed to address pediatric HIV/AIDS. One clear priority that emerged during the discussion was the importance of early identification and diagnosis of infants. Significant progress has been made to prevent mother-to-child transmission of HIV (PMTCT); however, many infants are still not receiving a HIV test after birth. In fact, in 2013 only 42% of infants born to HIV-positive mothers in low- and middle-income countries were tested for HIV within 2 months of life.

Additional steps are needed in order to ensure that all infants receive a HIV test, receive the results of that test, and if positive, are linked to care and treatment services. Successful testing, care and treatment programs currently exist to reach children infected with HIV, and, as noted by Charles Lyons, President and CEO of the Elizabeth Glaser Pediatric AIDS Foundation, investments need to be aimed at further scale-up of these services. However, Lyons also stressed that existing entry points are not reaching all HIV-exposed children and additional efforts are needed to identify HIV-infected and HIV-exposed children wherever and whenever they access health services. Identifying at-risk children at all entry points, such as maternal health facilities and nutrition sites, is also critical to early infant diagnosis. Scale up of these services will require healthcare workers not only to be trained specifically on how to identify and treat children, but also for healthcare workers to receive support and mentorship after training so that they can confidently address the unique needs of children – particularly young infants – on antiretroviral treatment.
Peter McDermott, Executive Director for the Children’s Investment Fund Foundation, emphasized that once children are tested and linked to care it is vital that every effort is made to retain those children in care. This requires tracking mother-baby pairs and making sure to provide support to caregivers of HIV-infected children. Supporting families and caregivers is crucial to achieving initiation and retention of children on treatment as they are responsible for bringing children to the clinics and encouraging children to adhere to treatment at home. In addition, increased investment needs to be made in stigma reduction programs. Stigma and discrimination limit one’s access to healthcare programs and make it more difficult to enroll and stay in care and treatment programs. Stigma does not only impact the HIV-positive individual, but often has an effect on family and caregivers. This is an important non-medical element in addressing the HIV pandemic in children.

The panel also argued that equal attention needs to be paid to pediatric drug development as is paid to early identification and enrollment on treatment. Deborah Birx, Ambassador at Large and U.S. Global AIDS Coordinator, noted that many of the existing formulations currently available for children are difficult to administer, may require refrigeration, have a heavy pill burden or bitter taste, all of which contribute to poor adherence. Shaffiq Essajee, Branch Chief for the Clinton Health Access Initiative, added that there are also fewer drugs available for children than adults and many of the existing fixed dose combination (FDC) drugs that are being used for treatment of children do not include the recommended drugs outlined in the recent World Health Organization global guidance. In addition, many children fail second line treatment options quickly and the science behind this treatment failure is still unclear. Investment in pediatric HIV drug development is critical if better quality drugs that meet the unique needs of children at different ages are to be made available.

Finally, Rajiv Shah, USAID Administrator, linked pediatric HIV investments with USAID’s child survival efforts. Approximately ½ of HIV-positive children will die by age two without treatment\(^5\), and HIV infected children get more frequent infections and have a higher fatality rate than HIV uninfected children.\(^6\) By better addressing the pediatric HIV pandemic overall child survival will improve. Panelists agreed that pediatric HIV/AIDS needs to be more strongly represented in child survival efforts in countries where maternal and pediatric HIV burden is high.

Ambassador Birx and Administrator Shah further discussed collaboration between USAID and PEPFAR to reach those children most vulnerable to morbidity and mortality and to ensure that health service delivery is targeted to areas with the highest HIV disease burden. There was agreement that cross referencing USAID and PEPFAR data to identify districts with high rates of under-five mortality and high HIV incidence would promote alignment of programmatic efforts in areas that would benefit from a more integrated health system approach. However, there was also agreement among panelists that even with improved interagency coordination, the success and sustainability of U.S.-funded efforts still depends heavily on national and local political leadership in country and increased domestic financing dedicated specifically to ending pediatric HIV and AIDS.

There were several priority areas highlighted throughout the first panel discussion where increased investment is needed, and if those investments are made, could have a profound impact on the pediatric HIV pandemic. Investment in pediatric HIV diagnostics, program scale up, healthcare worker training and caregiver support, stigma reduction, drug development, political will and programmatic innovation and collaboration are essential if the global community is going to further the fight against HIV/AIDS and better address the needs of children.
Gerson then transitioned to the second panel where new directions in basic and clinical pediatric HIV research and innovations in drugs and diagnostics for pediatric AIDS were discussed. Gwynn Stevens, Global HIV Virology Director for Cepheid, highlighted the importance of point of care (POC) diagnostics as a means for early infant diagnosis. POC diagnostics would help to speed up the testing process and improve turnaround time for results, in turn positively impacting the number of HIV-positive children who are identified and ideally linked to care and enrolled on treatment. She also specifically noted that POC diagnostic commodities must be “fit for purpose”, meaning the testing technologies should be appropriate for the conditions of the setting in which they will be used otherwise the technologies could be rendered useless.

The importance of pediatric drug research and development was also a key topic of discussion during the second panel. This included not only a discussion around the development of new drugs, but the improvement of existing drugs, the approval of those drugs for use in children, and identifying the appropriate dosing for use in children at different ages.
There was specific discussion on the development of long-acting drugs, with Lynne Mofenson, Branch Chief for the Maternal and Pediatric Infectious Disease Branch at NIH, noting the potential benefits for children due to their unique vulnerabilities to HIV. The development of long-acting drugs could help to provide protection to infants during the breastfeeding period as well as help with adherence for older HIV-positive children, since the drugs would not need to be taken as often. Panelists considered research on long-acting drugs for children a high-priority for potential investment.

It was also clear throughout the morning that not only are drug developments needed for new treatments, but continued research is essential in order to find a HIV vaccine or cure. José Esparza, Adjunct Professor at the University of Maryland, stressed the importance of vaccines – they are cost effective when compared with lifelong treatment, they provide protection from future infection, and there are successful immunization platforms that already exist in many countries and save millions of lives every year. Doug Nixon, Professor at The George Washington University, raised the point that basic research on pediatric HIV is still needed and what we learn from this research could catalyze pediatric HIV vaccine and cure research. Nixon also talked about how a HIV vaccine would help to protect HIV-negative children and could also be used for therapeutic purposes for HIV-positive children as a means to boost the immune system’s response and slow the disease progression. The development of a HIV vaccine or cure would truly be a game-changing innovation in the response to the pediatric HIV pandemic.

The development of drugs and vaccines for children naturally raises concerns about how and when children should be included in HIV/AIDS research. Esparza touched on the ethical considerations of including children in research and emphasized the importance of drug development for this specific population. Not including children in research can actually be more harmful to children due to the end result of fewer drugs being made available for them. There are regulations and federal procedures in place to address the ethical considerations of including children in trials, but these should not be seen as barriers to research – the inclusion of children in studies is critical to ensuring new drug developments and potential vaccines or cures are approved for use in children at the same time or soon after adults. It is also imperative that drugs be studied in children to ensure appropriate dosing levels for children, and the safety and efficacy of the drugs.

As evident through the second panel discussion, the importance of new innovations in HIV research is paramount. Increased funding in this area is essential to ensure that children remain a priority in the HIV/AIDS research agenda and that children benefit from advances designed specifically for their unique medical needs. The development of new FDCs for children, long-acting drugs, or a HIV vaccine or cure would significantly impact the pediatric HIV pandemic and turn the tide strongly toward an HIV-free generation.
The scientific and social aspects of fighting pediatric AIDS today

In the final session of the morning, Deborah Persaud, Professor of Pediatrics at Johns Hopkins University School of Medicine, discussed the case of the “Mississippi Baby”, the importance of early identification and treatment for infants, and the need for continued research in this field to help children in the United States as well as those abroad. Persaud is the lead investigator for the “Mississippi Baby” case, who until July 2014 was thought to have been “functionally cured” of HIV. Persaud discussed the importance of early identification and initiation on treatment in the case of the “Mississippi Baby” and the role it may have played in allowing the child to remain virally suppressed with no virus detection.

The child known as the “Mississippi Baby” was born to a HIV-positive mother who received no prevention of mother-to-child transmission of HIV (PMTCT) services prior to arrival at the hospital for delivery. Soon after birth, the child tested positive for HIV and was immediately started on a high dose of antiretroviral drugs. The child remained in care and on ART until 18 months of life, at which time she was lost to follow-up. Five months later the child returned to care, was examined by medical professionals and was found to have no evidence of HIV infection after extensive testing. The “Mississippi Baby” remained off treatment with undetectable viral load for more than 2 years and was thought to have been “functionally cured” of HIV. However, as learned after the June meeting, at the age of 4 the child began to show signs that the virus was replicating in her body and was immediately initiated on treatment. The “Mississippi Baby” is a sobering reminder that even in the United States, where quality health care services are available, children continue to be infected with HIV and challenges to accessing care and retaining children on treatment remain.

Additional research is needed in order to better understand why early initiation on treatment resulted in such a long period of viral suppression after treatment was stopped for the “Mississippi Baby”, when often HIV-positive children rebound within 2-4 weeks, as noted by Persaud. These findings could provide additional insight to a HIV-positive infant’s virus reservoir and immune response to this disease. Studying an infant’s immune response to HIV may even lead to better drug developments, including a HIV vaccine or a cure. There are still many unknowns in the field of HIV and pediatric specific research must continue if progress is to be made towards the elimination of pediatric HIV.
Thirty years into the AIDS pandemic, children continue to be left behind in global HIV/AIDS response. This roundtable event on ending pediatric AIDS reinforced the importance of gathering top scientists, advocates, government officials, donors, and implementing partners together in one room to collectively address the challenges facing the field of pediatric HIV. The roundtable also firmly established that considerable investment in pediatric-specific programs, policies and innovations is still needed in order for progress to continue.

We are at an important moment in the fight to end pediatric AIDS. Now more than ever the global community needs to put children at the center of the HIV/AIDS response and dedicate resources towards pediatric HIV research and development, program implementation and scale-up, and advocacy.

CONCLUSION