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Preventing measles in children and adolescents with HIV

Gurpreet Kaur[a,b], **Robert T. Perry**[a]

[a]Global Immunization Division, Center for Global Health, Atlanta, Georgia, USA.

[b]Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

Measles – clinically recognized as fever, rash and one or more of cough, coryza, or conjunctivitis – has been a leading cause of vaccine-preventable disease and death. Despite the existence of a well tolerated and effective vaccine, an estimated 128 000 children worldwide died of measles in 2021 [1]. Measles complications typically include pneumonia and diarrhea, caused either directly by measles virus or indirectly by measles-induced loss of preexisting immunity to common childhood pathogens [2–5]. Among people with HIV (PWH), measles infection can lead to severe pneumonia, encephalitis, and death; among children with HIV (CHIV), the mortality risk doubles [3,6].

For infants exposed to HIV *in utero* or HIV-infected but asymptomatic, WHO recommends a supplementary measles vaccine dose at 6 months of age in addition to the doses routinely recommended by the country's immunization schedule [7]. A measles vaccine dose at 6 months aims to vaccinate these infants soon after they lose maternally derived antibodies and while HIV-infected infants are better able to develop an immune response [8,9]. Although immune reconstitution during antiretroviral therapy (ART) does not restore preexisting measles immunity [10], vaccination after reconstitution can induce protective immunity against measles [11,12]. WHO therefore recommends providing at least one measles vaccine dose after immune reconstitution following ART initiation, or 6–12 months after ART initiation when $CD4^+$ testing is not available [7].

Although maternal-to-child-transmission of HIV has decreased remarkably over the last decade, an estimated 160 000 new HIV infections occurred globally in children aged 0–14 years in 2021. In 2021, an estimated 800 000 CHIV were not receiving ART, over half in eastern and southern African countries, and, among children on ART, nearly half did not achieve viral suppression [13]. The 2016 ZAMPHIA found that 99% of HIV-infected women (aged 15–49 years) were receiving ARTat time of delivery and that, among these HIV-infected women, regardless of ART use, 7.7% of their infants, born in the 17 months preceding the survey, were infected with HIV. Among children aged 0–14 years in the ZAMPHIA, HIV prevalence was estimated at 1.1%. Parents of 47% of CHIV aged 0–14 years reported they knew the child's HIV status and further 90% reported the child was on

Correspondence to Robert T. Perry, MD, MPH, Global Immunization Division, Center for Global Health, Centers for Disease Control and Prevention, 1600 Clifton Rd NE Mailstop H26-1, Atlanta, GA 30329, USA. rmp9@cdc.gov.

Conflicts of interest

There are no conflicts of interest.

ART. Fifty-three percent of HIV-infected children aged 0–14 years in ZAMPHIA showed viral load suppression [14].

In this issue of *AIDS*, Mutembo *et al.* [15] describe the results of measles and rubella serologic testing of samples collected for the 2016 Zambia Population HIV Impact Assessment (ZAMPHIA). They found that HIV-infected children younger than 10 years have much lower rates of measles seropositivity than HIV-uninfected children. Similar findings had previously been obtained from smaller studies with nonrepresentative samples in specific populations [15,16]. Although 74% measles seroprevalence in HIV-negative children appears close to expected based on measles vaccination coverage in the years before the ZAMPHIA survey, seroprevalence was only 47% in CHIV. The survey also provided reassuring results that rubella seropositivity was high in both HIV-infected and uninfected older adolescents and adults prior to national rubella vaccine introduction. Because vaccination history was not included in the ZAMPHIA and up to 16% of children lacked information on ART, Mutembo et al. [15] could not assess whether WHO recommendations had been followed.

These results from Mutembo *et al.* [15] and the ZAMPHIA survey suggest possible gaps in implementing current WHO recommendations for measles vaccination in CHIV. The lower rate of measles seropositivity among HIV-infected children younger than 10 years likely represents some combination of failure to vaccinate or vaccine failure. Children born to women with HIV may not be receiving the earlier dose of measles vaccine at 6 months of age nor at the standard ages of 9 and 18 months per the Zambia immunization schedule [17]. In addition, CHIV may not receive a measles vaccine dose after immune reconstitution because not all HIV-exposed children are tested, or if they are tested, then those found to have HIV are not starting ART; or if they start ART, then they are not being revaccinated after immune reconstitution.

Identifying and closing these gaps will require close coordination between immunization and HIV programs to provide timely measles vaccination and ART to CHIV. Although ART has improved long-term survival in PWH, studies in India, Niger, South Africa, Uganda, and Zambia suggest continued challenges reaching CHIV with immunization services, including missed opportunities for vaccination during visits for HIV services [18–22]. Although few studies have examined the underlying reasons for lower immunization among CHIV, possible contributing factors include debilitating maternal HIV illness preventing routine childcare activities, lack of money to access clinic services, fear of stigma at clinic, and/or lack of awareness of vaccination benefits [20,21,23].

In many African countries, the last recommended infant vaccination is in the second year of life, and national vaccine policies and practices are not to vaccinate children older than 24 months of age with measles or any other routine vaccination [24], except during mass vaccination campaigns. Ideally, children should be diagnosed with HIV and receiving ART well before 2 years of age [25], but those who start ART later should still be able to receive life-saving vaccines, even if older than 24 months [26,27]. Ministries of Health could consider examining their immunization policies and practices to permit measles vaccination of PWH past the routine immunization age [7]. Policy and practice changes could be

required to provide all children routine vaccinations they missed during the years since the start of the COVID-19 pandemic [24]. Country programs could exploit the opportunity presented by the postpandemic recovery of health systems to better integrate HIV and vaccination services.

The findings of Mutembo *et al.* [15] reinforce the benefits to countries working toward measles and HIV elimination of integrating measles and other routine vaccinations in the package of care for CHIV. This integration starts with stronger collaboration between country immunization and HIV programs for practical reinforcement of WHO guidance such as providing life-saving immunizations during follow-up of CHIV, whether at dedicated HIV or integrated child health clinics, as well as policy changes to enable vaccine access outside standard routine immunization schedules' age ranges.

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