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Research on very early ART in neonates at risk of HIV infection

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The continued importance of research on very early ART in neonates at risk of HIV infection

The Mississippi child, previously in sustained viral remission, now has detectable levels of HIV.¹ This news is profoundly disappointing. We write this correspondence to clarify that research on the use of very early antiretroviral therapy in infants born to HIV-infected mothers is still important. This development, however, gives reason to think carefully about how to conduct this research.

Although the Mississippi case did not demonstrate how to achieve a cure for HIV, it is the first documented case where an individual infected with HIV was able to remain free of detectable HIV for a sustained period of time, despite not being on antiretroviral treatment (ART) and not being an elite controller.² Independent evidence, including animal data,³ evidence from adult cohorts initiating ART in acute infection,⁴ and data on post-exposure prophylaxis in adults,⁵ suggests that very early combination ART (whether alone or in conjunction with other interventions) might enable infants to avoid a lifetime of ART. Nevertheless, it is not yet certain why the Mississippi child experienced viral remission for more than two years, why the virus reemerged, or whether modifications of this strategy may lead to longer periods of remission (which would offer the benefit of avoiding antiretroviral therapy and the associated side effects).

Research on the use of very early combination therapy in infants of HIV-infected mothers to achieve viral remission therefore remains critically important, as is the question of how to maintain potential lifelong viral remission. We believe the ethical framework in our accompanying article is still the right approach for proceeding with this research. The challenge lies in specifying appropriate adjustments to the scientific plan and the ethical safeguards in light of this new information. For instance, perhaps the Mississippi child was not on treatment long enough to achieve lifelong viral remission, but it is not clear how long treatment should be given for the strategy to work. This suggests an even greater need for an ongoing process in which experts reach consensus on criteria for discontinuing and for restarting treatment based on this new information and other future developments. These criteria will need to be rigorous enough to protect the individual children participating in research *and* to have the best chance of answering the question about whether very early therapy can lead to sustained viral remission of HIV.

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