with detection of SARS-CoV-2 in the cerebrospinal fluid (CSF). In this case, the *Quick*-DNA/RNA Viral MagBead (Zymo Research Corp, Irvine, CA) extraction kit on the automated KingFisher Flex Purification System (Thermo Fisher Scientific, Waltham, MA) was used for nucleic acid extraction and the Allplex nCoV-2019 kit (Seegene, Inc., Seoul, South Korea) for gene amplification. Moreover, appropriate positive, negative and internal controls were used to add confidence in the results. The multiplex real-time RT-PCR assay used in this case has a limit of detection of 4167 copies/ml and a sensitivity of 100 copies/reaction. Target genes amplified within ≤40 cycle threshold were considered detected, and the patient had a positive result for the presence of SARS-CoV-2 RNA in the CSF.

Regarding the possibility of repeating the CSF virus investigation during follow-up, we decided not to perform invasive procedures with exclusively academic purpose, as this would not change the therapeutic approach. In addition, brain magnetic resonance imaging (MRI) was normal and the patient did not show any signs of brain involvement suggestive of Bickerstaff encephalitis, such as external ophthalmoplegia or disturbance of consciousness. Respiratory muscles were not involved nor did the patient had autonomic dysfunction. The symptoms presented by the patients were explained in the article.

Finally, it is worth remembering that during the recent Zika and Chikungunya epidemics, viral RNA was also found in CSF of patients with Guillain-Barré syndrome, as well as the presence of IgM and IgG.[2] According to Parra et al,[3] arbovirus-related GBS may be caused by direct infection or parainfectious nerve damage, due to the short time between onset of infectious and neurologic symptoms. Although direct viral invasion is a less likely pathophysiologic mechanism for a disease classically defined as immune-mediated, the presence of SARS-CoV-2 RNA in CSF makes it impossible for us to rule out this hypothesis.

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The authors have no funding or conflicts of interest to disclose.
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ISSN: 0891-3668/21/4012-e527
DOI: 10.1097/INF.0000000000003298

Remdesivir, Sinus Bradycardia and Therapeutic Drug Monitoring in Children With Severe COVID-19

To the Editors:

We would like to thank Eleftheriou et al[1] for their observation of sinus bradycardia in children treated with remdesivir (RDV) for COVID-19 and report similar findings in 3 of 4 children with severe COVID-19 who received RDV on our pediatric intensive care unit. We treated 2 boys with underlying chronic conditions (11 years with advanced neuronal ceroid lipofuscinoses type 2 and 13 years with primordial dwarfism) with RDV suffering from COVID-19 pneumonia, progressive demand for oxygen and high SARS-CoV-2 RNA copy number in nasopharyngeal swaps. The first patient developed episodes of sinus bradycardia on day 3 and day 4 on RDV (heart rate dropped to 59 bpm from 90 to 100 baseline), the second on day 5 (56 bpm from >100 baselines) when catecholamines were also withdrawn. Both patients survived but suffer from residual lung damage aggravating their chronic disease. In addition, significant sinus bradycardia (38 bpm from >100 baseline) also occurred on day 5 of RDV treatment in the first of 2 girls (7 years with dystrophy, mild microcephaly and hypothyroidism and 4 years with adipositas) who developed critical COVID-19 disease. In this girl, however, severe myocarditis leading to the need for extracorporeal life support (ECLS), hemofiltration, catecholamine-dosing and multiple other drugs could also have led to bradycardia.[2] Notably, in this patient, levels of RDV on day 5 and day 6 (2531 and 1938 ng/ml 1 h post-infusion, respectively) and its metabolite GS-441524 (trough level 239.5 and 291 ng/ml, respectively) were confirmed to be within target levels during ECLS and hemofiltration by the UHPLC-MS/MS method.[3] Sadly, both girls on ECLS finally succumbed due to fulminant COVID-19 despite multi-disciplinary intensive care. All children received 5 mg/kg RDV on the first day, followed by 2.5 mg/kg as considered to be safe and effective for compassionate use in children with severe COVID-19.[4]

We agree with Eleftheriou et al that physicians should be aware of potential cardiovascular adverse effects of RDV and use continuous cardiac monitoring and therapeutic drug monitoring in selected cases when treating children, especially in those with pre-existing cardiac conditions. Notably, catecholamine treatment and withdrawal can either mask or lead to bradycardia itself.

To the best of our knowledge, there are currently no other antiviral drugs (including monoclonal antibodies) to fight SARS-CoV-2 with at least some clinical experience in children and none are expected to receive marked authorization in the near future as clinical trials focus on participants 12 years

The authors have no funding or conflicts of interest to disclose.
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ISSN: 0891-3668/21/4012-e528
DOI: 10.1097/INF.0000000000003309

and older. Hence, we are left with the blanket statement that children are spared from severe COVID-19, an argument that is currently being used in many European countries, including the UK and Germany, to not vaccinate adolescents. Although few children become severely ill from SARS-CoV-2 infection compared with adults, the increasing number of delta variant infections will most likely result in preventable morbidity and mortality in this age group. Therefore, we call not only for pediatric clinical trials of antiviral drugs but, more importantly, for universal access to COVID-19 immunization for children and adolescents as safe and effective vaccines become licensed and available.[5]

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Sustaining Early Infant Diagnosis of HIV During Coronavirus Disease 2019 Pandemic

Experience Collecting Dry Blood Spots Samples at Home From HIV-exposed Infants in Nigeria

To the Editors:

Despite advances in prevention of mother to child transmission (PMTCT) of HIV, 160,000 new pediatric HIV infections were reported in 2020.[1] Vertical transmission of HIV in Nigeria remains high at 22%, with 37,000 new infections among children 0–14 years annually.[2] In Nigeria, access to early infant diagnosis (EID) has improved significantly; however, only 27% of HIV-exposed infants received an HIV test by 2 months of age in 2019.[3] EID programs require mothers to bring their infants to the health facility for testing. However, the global coronavirus disease 2019 (COVID-19) pandemic movement restrictions necessitated changes to the PMTCT service delivery model for infant follow-up to ensure uninterrupted service delivery.

Nigeria reported its first COVID-19 case on February 27, 2020.[4] By March, a mandatory lock down with subsequent movement restrictions limited access to health facilities for nonemergency presentations including PMTCT services.[4] The Reaching Impact Saturation and Epidemic (RISE) Control program, which currently provides comprehensive HIV prevention, care and treatment services to over 82,000 recipients of care, rapidly pivoted to a community service delivery model to ensure uninterrupted access to HIV services. To circumvent the challenges faced by mothers and caregivers in accessing health facilities during the COVID-19 lockdown period, RISE deployed trained nurses to collect dried blood spot (DBS) samples for HIV viral load and EID in the communities where children, infants and their caregivers live. EID samples were collected by trained nurses in the home and transported to the health facility for onward transportation to regional labs. When sample collection was not feasible in the home, caregivers were escorted to the nearest health facility for sample collection. Case managers also provided antiretroviral drug refills for recipients of care in the community including antiretroviral prophylaxis refills for infants.

Prelock down (October 2019 to March 2020), RISE collected 690 samples of which 57% (393/690) were collected within 2 months of birth with average turnaround time of 30 days. Postlock down (April to September 2020), 634 samples were collected of which 60% (379/634) were within 2 months of birth while maintaining an average turnaround time of 34 days. Regarding actual tests done, prelock down tests were done for 75% of samples for infants <2 months (n = 295) with 1.0 % positivity rate, while postlock down, 77% (n = 291) were tested with 0.3% positivity.

Early results from the RISE program have shown that DBS specimens for HIV diagnosis in infants can be safely collected at home while maintaining specimen integrity and delivery of results back to caregivers. Several adaptations have been made to HIV programming to improve service delivery for HIV-infected pregnant, breastfeeding women, infants, children and adolescents.[4] We propose that HIV programs consider implementing home-based DBS collection to increase access to timely EID services for HIV-exposed infants both as an adaption during the COVID-19 pandemic and as an enduring solution thereafter.

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The authors have no funding or conflicts of interest to disclose.
O.F. and T.Y. are cofirst authors.
The activities described were made possible with support from the US President's Emergency Plan for AIDS Relief, through the US Agency for International Development (USAID) funded Reaching Impact, Saturation, and Epidemic (RISE) Control program, under the terms of the cooperative agreement 7200AA19CA00003. The contents are the responsibility of the RISE program and do not necessarily reflect the views of USAID or the US Government.
This analysis falls under the nonresearch determination provided by Johns Hopkins School of Public Health Institutional Review Board number 8634 under the protocol "Secondary Data Analysis of HIV Prevention, Care and Treatment Service Delivery Programs in Africa."
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ISSN: 0891-3668/21/4012-e535
DOI: 10.1097/INF.0000000000003306