we recognize the extreme difficulties in obtaining lower respiratory tract specimens in this setting, this does pose a barrier to attributing causality to CMV.

Additionally, the authors reported CMV DNAemia as copies per milliliter. The World Health Organization International Standard for CMV recommends calibrating results to international units per milliliter in order to prevent large interlaboratory heterogeneity. This variability is not only problematic for laboratories but also clinicians and patients and can be as large as 6 $\log_{10}$ [9, 10]. Therefore, reported DNAemia values are difficult to interpret, and viral loads cannot be translated into other settings.

Considering these points, CLD is likely to have a multifactorial etiology in this population. Although an interesting hypothesis, an independent association between CMV DNAemia and CLD remains unconfirmed in this population. We agree that further work is required to refine our understanding of CMV DNAemia and CLD. This will require sampling the lower respiratory tract, calibrating quantitative CMV viral load results to the international standards, and including other relevant potential confounders in time-varying multivariable analysis, which are necessary to determine if trials of antivirals against CMV in this particular setting are warranted.

Note

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Muge Cevik,[1,2,3] Clark D. Russell,[2,4] and David S. Y. Ong[5,6]

[1]Division of Infection and Global Health Research, School of Medicine, University of St Andrews, and [2]Regional Infectious Diseases Unit, Western General Hospital, NHS Lothian, [3]Department of Laboratory Medicine, Royal Infirmary of Edinburgh, and [4]University of Edinburgh Centre for Inflammation Research, Queen's Medical Research Institute, Edinburgh BioQuarter, United Kingdom; and [5]Department of Medical Microbiology and Infection Control, Franciscus Gasthuis & Vlietland, Rotterdam, and [6]Department of Epidemiology, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, The Netherlands

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Correspondence: M. Cevik, Division of Infection and Global Health Research, School of Medicine, University of St Andrews, Fife, KY16 9TF (mc349@st-andrews.ac.uk).

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Reply to Cevik et al

To the Editor—We thank Cevik and colleagues for their interest in our recent report and acknowledge that they raise some caveats about our study.

The first issue raised is that there may be other confounding factors that could explain the observed association between the presence of cytomegalovirus (CMV) DNAemia and chronic lung disease (CLD), which were not addressed in our analysis. We acknowledged this limitation in the Discussion section of our article, noting, for example, that the lack of available human immunodeficiency virus (HIV) viral loads for participants in this study raised the possibility that the study subjects with high levels of CMV DNAemia might also be those with raised HIV loads, probably as a result of poor adherence. We also made it clear that an association study cannot ascribe causation and thus it was equally plausible that elevated CMV DNA levels and comorbidities such as stunting and CLD were each independent markers of progressive perinatally acquired HIV (PHIV) disease.

Nevertheless, we believe that there is some biological plausibility to the suggestion that CMV could contribute to the pathogenesis of CLD. Although Cevik and colleagues are correct in saying that many older HIV-infected children present with CLD following a history of frequent respiratory infections (and may have radiological features of bronchiectasis), the pathognomonic features on high-resolution computed tomographic scanning are more in keeping with small airways disease, characteristic of the inflammatory condition obliterative bronchiolitis, which in children frequently has a viral etiology and often follows a severe viral lower respiratory tract infection in the early years of life [1]. CMV is a common cause of pneumonitis in early life in children living with HIV [2], and CMV DNAemia is strongly associated with CMV lung disease in infants infected with HIV [3], consistent with our hypothesis. However, we certainly acknowledge that further studies, including sampling of bronchoalveolar lavage fluid and/or tissue, would be very important in establishing a potential relationship between CMV and CLD in children with PHIV. The scarcity of local facilities for pediatric bronchoscopy has so far made this difficult to investigate in Harare.

The authors are also concerned about the reporting of CMV DNA as copies/mL rather than international units (IU)/mL, which they say may make extrapolation of our data problematic. We are certainly aware that interpretation of CMV DNA data in clinical settings around the world is not a trivial undertaking. We used an internationally recognized and highly sensitive testing algorithm for our experiments, employing the RealStar CMV polymerase chain reaction (PCR) kit 1.0 (based on real-time PCR technology) to detect and quantify CMV DNA. The analytical performance of this kit was determined using a dilution series (10^0–10^9 IU/μL) of quantified CMV-specific DNA from the first WHO International Standard for Human Cytomegalovirus for nucleic acid amplification techniques (National Institute for Biological Standards and Control code 09/162). The analytical sensitivity (limit of detection) was defined as the concentration of CMV DNA molecules that can be detected with a 95% positivity rate. Using the Applied Biosystems real-time PCR instruments, the limit of detection for the RealStar CMV kit was 0.668 IU/μL (95% confidence interval, .323–2.258 IU/μL). All of our results were obtained automatically from the instrument in IU/mL, but we used a conversion factor (as specified in the Supplementary Methods, "the conversion factor for DNA values to copies/mL was 0.6") to allow more widespread use of the data. We apologize if that was not clear to the readers.

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Sarah Rowland-Jones,[1] Louis-Marie Yindom,[1] and Rashida Ferrand[2,3]

[1]Nuffield Department of Medicine, University of Oxford, and [2]London School of Hygiene and Tropical Medicine, United Kingdom; and [3]Biomedical Research and Training Institute, Harare, Zimbabwe

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Correspondence: S. Rowland-Jones, NDM Research Bldg, Nuffield Department of Medicine, University of Oxford, Old Road Campus, Roosevelt Drive, Headington, Oxford OX3 7FZ, UK (sarah.rowland-jones@ndm.ox.ac.uk).

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Is *Mycobacterium chimaera* Infection After Cardiac Surgery a Risk Factor for Bacterial Prosthetic Valve Endocarditis?

To the Editor—We congratulate Kasperbauer and Daley for their precious guide to diagnosis and management of *Mycobacterium chimaera* infections related to contaminated heater-cooler units published in the April 1 issue of *Clinical Infectious Diseases* [1].

M. chimaera causes severe prosthetic valve endocarditis (PVE) and disseminated infections late after open heart surgery, with an estimated risk of 1/1000 patient in hospital where infections have been identified [2, 3]. PVE by conventional bacteria is also a relatively rare disease, occurring in 1–6% of prosthetic valve implantations, with a 0.4% annual risk from 12 months after surgery [4]. Here we want to bring to attention how *M. chimaera* infection should be considered after diagnosing a PVE from conventional bacteria, by reporting the last case of *M. chimaera* PVE diagnosed at our hospital.

In March 2019, a 75-year-old male was admitted with a 6-month history of fever and psychophysical decay. In 2016, the patient underwent bioprosthetic aortic valve replacement. On admission, pertinent laboratory findings included mild anemia and elevated serum creatinine. The transesophageal echocardiogram (TOE) revealed endocarditis vegetations on the cusps of the bioprosthetic valve with severely elevated transvalvular gradients. Either conventional and mycobacterial blood cultures performed at entry grew *Enterococcus faecalis* after few days. The patient received intravenous ampicillin and ceftriaxone therapy for 6 weeks, with retention of the bioprosthetic valve. At the end of therapy, TOE demonstrated a significant improvement of the valvular function. However, repeated mycobacterial blood cultures collected in the second week of therapy turned out positive for *M. chimaera* after 6 weeks. The patient started a 4-drug antimycobacterial regimen with azithromycin, rifabutin, ethambutol, and clofazimine, while maintaining suppressive antibiotic therapy with amoxicillin.

Our case shows that mycobacterial blood cultures can be contaminated by conventional fast-growing bacteria, and in cardiac surgery patients at risk for *M. chimaera* infection, diagnosing a PVE from conventional bacteria does not exclude a concomitant *M. chimaera* infection. Indeed, our limited data seem to indicate a particularly high risk of bacterial PVE in patients with *M. chimaera* infection: in the last 3 years, we have identified 7 patients with *M. chimaera* infections after cardiac surgery (Table 1). For 3 out of 7 patients, the diagnosis of *M. chimaera* infection was preceded 1–6 months earlier by a PVE from conventional bacteria according to Duke's criteria, and all the patients improved transiently with targeted antibiotic therapy [5].