single mutants (i.e., BA.2\_L452Q and BA.2\_ S704L) had neutralizing-antibody escape that was similar to that of the BA.4/5 and BA.2.12.1 subvariants, with neutralizing-antibody titers that were 14.1% and 26.6% lower, respectively, than those against BA.2 (P>0.05 for both comparisons) (Fig. 1D). Notably, 2 of 30 BA.1-infected but unvaccinated patients (Patients U12 and U13) had high neutralizing-antibody titers against all the variants except BA.4/5, whereas patients who had received a booster dose had broader neutralization against all the variants examined (Fig. S3C and S3D). Overall, these results showed that infection during the BA.1 wave did not appear to offer effective protection against the newly emerged sublineages.

In this study, we characterized infectioninduced immunity and vaccine-induced immunity against newly emerged omicron subvariants. Booster vaccination provided sufficient neutralizing-antibody titers against the BA.4/5 and BA.2.12.1 subvariants, albeit to a lower extent than against BA.1 and BA.2.<sup>4,5</sup> These findings underscore the importance of booster vaccination for protection against emerging variants.

Panke Qu, M.S. Julia Faraone, B.S. Shan-Lu Liu, M.D., Ph.D. Ohio State University Columbus, OH liu.6244@osu.edu and Others Mr. Qu, Ms. Faraone, and Mr. Evans contributed equally to this letter.

A complete list of authors is available with the full text of this letter at NEJM.org.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Supported by a fund provided by an anonymous donor to Ohio State University (to Dr. Liu); an award (U54CA260582, to Drs. Lozanski, Saif, Oltz, Gumina, and Liu) from the National Cancer Institute of the National Institutes of Health (NIH); a grant (R01 A1150473, to Dr. Liu) from the NIH; a Glenn Barber Fellowship (to Mr. Evans) from the Ohio State University College of Veterinary Medicine; grants (to Dr. Gumina) from the Robert J. Anthony Fund for Cardiovascular Research and the JB Cardiovascular Research Fund; a grant (R01 HD095881, to Dr. Saif) from the NIH; and grants (UL1TR002733 and KL2TR002734, to Dr. Bednash) from the National Center for Advancing Translational Sciences.

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

This letter was published on June 15, 2022, at NEJM.org.

1. Centers for Disease Control and Prevention. COVID data tracker: variant proportions (https://covid.cdc.gov/covid-data -tracker/#variant-proportions).

2. National Institute for Communicable Diseases South Africa. SARS-CoV-2 genomic surveillance update: tracking SARS-CoV-2 variants (https://www.nicd.ac.za/diseases-a-z-index/disease-index -covid-19/sars-cov-2-genomic-surveillance-update/).

3. Zeng C, Evans JP, Pearson R, et al. Neutralizing antibody against SARS-CoV-2 spike in COVID-19 patients, health care workers, and convalescent plasma donors. JCI Insight 2020; 5(22):e143213.

**4.** Evans JP, Zeng C, Qu P, et al. Neutralization of SARS-CoV-2 omicron sub-lineages BA.1, BA.1.1, and BA.2. Cell Host Microbe 2022 April 25 (Epub ahead of print).

5. Pajon R, Doria-Rose NA, Shen X, et al. SARS-CoV-2 omicron variant neutralization after mRNA-1273 booster vaccination. N Engl J Med 2022;386:1088-91.

DOI: 10.1056/NEJMc2206725

## **Detection of Marburg Virus Disease in Guinea**

TO THE EDITOR: On August 2, 2021, a 46-yearold man from Temessadou M'Boké, a village in Guéckédou prefecture in Guinea, died after hemorrhaging from several natural orifices. On August 3, an initial diagnosis of Marburg virus (MARV) infection was made after real-time reversetranscriptase-polymerase-chain-reaction testing of a postmortem buccal sample obtained from the patient was performed and revealed a cyclethreshold value of 13.4 (Fig. 1A). Field investigation teams were deployed, and the diagnostic finding was validated in two additional laboratories within a few days. In-country metagenomic next-generation sequencing allowed for full-length MARV genome recovery (99.3%), and phylogenetic analysis indicated that the new

Guinea MARV strain that had been identified in the patient clustered with MARV strains isolated from bats in Sierra Leone and from humans in Angola (Fig. S1 and Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Close monitoring for a period of 21 days confirmed that all the patient's contacts had remained asymptomatic, and no additional cases were detected.

Guinean forests, along with other areas of West Africa, including Sierra Leone, are thought to be environmentally suitable for zoonotic transmission of Marburg virus disease by bats and particularly by *Rousettus aegyptiacus* (Egyptian fruit bat), which has been identified as a natural MARV reservoir host (Fig. 1B).<sup>1-3</sup> Among the bat

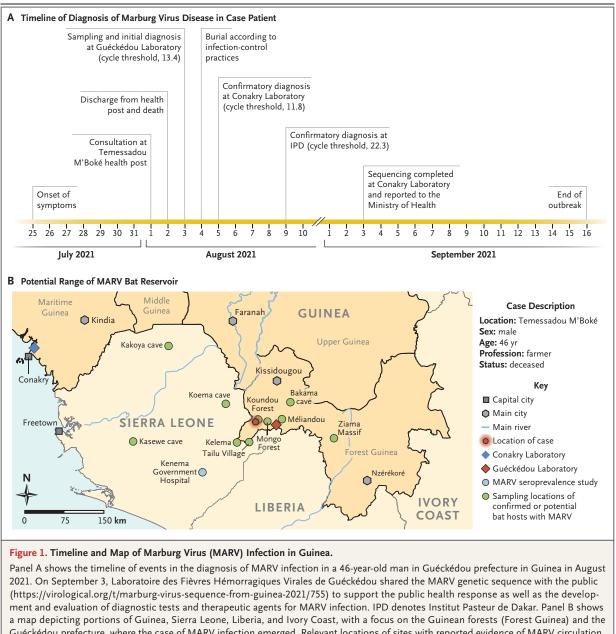
N ENGL J MED 386;26 NEJM.ORG JUNE 30, 2022

The New England Journal of Medicine

Downloaded from nejm.org on July 10, 2022. For personal use only. No other uses without permission.

Copyright © 2022 Massachusetts Medical Society. All rights reserved.

### CORRESPONDENCE



Guéckédou prefecture, where the case of MARV infection emerged. Relevant locations of sites with reported evidence of MARV circulation in bats and in humans in Sierra Leone are shown, along with sites in Guinea where bat species that are known to be potential reservoir hosts of MARV have been identified, including Méliandou (the location of the 2014-2016 Ebola virus disease outbreak), as well as Mongo Forest, Koundou Forest, Bakama cave, and Ziama Massif. Details regarding the mapping procedure are provided in the Supplementary Appendix.

in a household of four people. There was no evidence of a travel history outside Guinea for

reservoirs of MARV is Koundou, which is close in close contact with nature and wildlife and to the location where the case emerged. The may therefore have had repeated exposure to an patient had limited social interactions and lived environment or food contaminated with excreta of MARV-infected bats. Community surveys showed that although he may have harvested the patient or his close contacts or of contact wild fruits for personal consumption, there was with returning travelers. He was a farmer living no suggestion that he had visited caves or been

N ENGL J MED 386;26 NEJM.ORG JUNE 30, 2022

The New England Journal of Medicine Downloaded from nejm.org on July 10, 2022. For personal use only. No other uses without permission. Copyright © 2022 Massachusetts Medical Society. All rights reserved.

### The NEW ENGLAND JOURNAL of MEDICINE

involved in hunting activities for bushmeat, including bats. Traditional practices of bushmeat consumption or preparation (i.e., direct exposure to body fluids) cannot be fully excluded, since it is unlikely that such exposures would have been disclosed owing to the national ban on such consumption that had been enforced after the 2021 outbreak of Ebola virus disease.

The new Guinea MARV and the Angola MARV clade share a common ancestor that probably existed in 1965 (95% confidence interval, 1944 to 1981 on Bayesian molecular clock analysis). This finding indicates that approximately 55 years ago, these lineages diverged from a common ancestor, and each evolved independently in its respective reservoir host, with the presence of the Guinea MARV remaining undetected until this 2021 spillover event. This timescale of decades provided ample opportunity for the virus to be dispersed over large distances by bat migration. A parallel could be drawn with the emergence of the West African Ebola virus lineage (Makona) that diverged from a central African ancestor and independently evolved in its host until the spillover event happened.<sup>4</sup> In the case of MARV, the basal clustering of bat MARV in Sierra Leone suggests that even the Angola outbreak may have had its roots in West Africa.

Both the epidemiologic features and phylogenetic history argue against the possibility that the newly emerging MARV might have been imported. Overall, it seems plausible that the viral emergence in Guinea was due to a zoonotic transmission event from a bat reservoir at the end of July 2021.

The patient's isolated lifestyle probably played a role in minimizing the risk of secondary infections. Notably, a timely laboratory diagnosis was facilitated by the establishment of capacitybuilding programs, long-term collaborative partnerships, and decentralized laboratories with well-trained staff members. The same capacities proved to be key during the recent reemergence of Ebola virus disease in Guinea.<sup>5</sup>

Fara R. Koundouno, M.Sc. Bernhard Nocht Institute for Tropical Medicine Hamburg, Germany Liana E. Kafetzopoulou, Ph.D. KU Leuven Leuven, Belgium Martin Faye, Ph.D. Institut Pasteur de Dakar Dakar, Senegal Annick Renevey, Ph.D. Bernhard Nocht Institute for Tropical Medicine Hamburg, Germany

Barrè Soropogui, M.Sc. Université Gamal Abdel Nasser Conakry, Guinea

Kékoura Ifono, B.Sc. Emily V. Nelson, Ph.D.

Bernhard Nocht Institute for Tropical Medicine Hamburg, Germany

Aly A. Kamano, M.P.H., M.D. World Health Organization Guinea Conakry, Guinea

Charles Tolno, M.P.H., M.D.

Médecins sans Frontières Belgium Conakry, Guinea

Giuditta Annibaldis, Ph.D. Saa L. Millimono, B.Sc.

Bernhard Nocht Institute for Tropical Medicine Hamburg, Germany

Jacob Camara, Pharm.D.

Université Gamal Abdel Nasser Conakry, Guinea

Karifa Kourouma, B.Sc.

Bernhard Nocht Institute for Tropical Medicine Hamburg, Germany

Ahmadou Doré, B.Sc. Université Gamal Abdel Nasser Conakry, Guinea

Tamba E. Millimouno, B.Sc. Fernand M.B. Tolno, B.Sc.

Julia Hinzmann, M.L.T.

Hugo Soubrier, M.Sc. Mette Hinrichs, M.L.T.

Anke Thielebein, Ph.D.

Glaucia Herzer, M.Sc.

Meike Pahlmann, Ph.D.

Bernhard Nocht Institute for Tropical Medicine Hamburg, Germany

Georges A. Ki-Zerbo, M.D. World Health Organization Guinea

Conakry, Guinea

Pierre Formenty, D.V.M. Anaïs Legand, M.P.H.

World Health Organization

Geneva, Switzerland

Michael R. Wiley, Ph.D. University of Nebraska Medical Center Omaha, NE

Ousmane Faye, Ph.D. Moussa M. Diagne, Ph.D. Amadou A. Sall, Ph.D. Institut Pasteur de Dakar Dakar, Senegal

N ENGLJ MED 386;26 NEJM.ORG JUNE 30, 2022

The New England Journal of Medicine

Downloaded from nejm.org on July 10, 2022. For personal use only. No other uses without permission. Copyright © 2022 Massachusetts Medical Society. All rights reserved.

#### CORRESPONDENCE

Philippe Lemey, Ph.D. KU Leuven

Leuven, Belgium Aïssatou Bah, B.Sc. Université Gamal Abdel Nasser

Conakry, Guinea Stephan Günther, M.D., Ph.D.

Bernhard Nocht Institute for Tropical Medicine Hamburg, Germany

Sakoba Keita, M.D. Agence Nationale de Sécurité Sanitaire Conakry, Guinea

Sophie Duraffour, Ph.D. Bernhard Nocht Institute for Tropical Medicine Hamburg, Germany duraffour@bnitm.de

N'Faly Magassouba, Ph.D.

Laboratoire des Fièvres Hémorragiques Virales de Guinée Conakry, Guinea

Ms. Koundouno and Dr. Kafetzopoulou and Drs. Duraffour and Magassouba contributed equally to this letter.

Supported by the German Federal Ministry of Health through an agreement (ZMV 11-2517WH0005) with the World Health Organization (WHO) Collaborating Center for Arboviruses and Hemorrhagic Fever Viruses at the Bernhard Nocht Institute for Tropical Medicine and agreements (ZMV 11-2517GHP-704, ZMV11-2519GHP704, and ZM11-2521GHP921) with the Global Health Protection Program; by grants (GU883/5-1 and GU883/5-2) from the German Research Foundation; by a research and innovation grant agreement (871029-EVA-GLOBAL) with the European Union's Horizon 2020; by the Coalition for Epidemic Preparedness Innovations (CEPI-ENABLE); and by a grant agreement (R1A2016E-1609) with the PANDORA-ID-NET of the European and Developing Countries Clinical Trials Partnership. The Bern hard Nocht Institute for Tropical Medicine is a member of the German Center for Infection Research (partner site in Hamburg, Germany), which provided support for this study. The European Mobile Laboratory in coordination with the Bernhard Nocht Institute for Tropical Medicine is a technical partner of the WHO Global Outbreak Alert and Response Network (GOARN); the deployment of the European Mobile Laboratory to Guinea has been coordinated and supported by the GOARN Operational Support Team at WHO. Dr. Lemey is supported by a grant agreement (725422-ReservoirDOCS) with the European Research Council under the European Union's Horizon 2020 and by grants (G066215N, G0D5117N, and G0B9317N) from the Research Foundation-Flanders and by funding from the Wellcome Trust through the Artic Network project (206298/Z/17/Z). The work of Institut Pasteur de Dakar was supported in part by PraesensBio of Lincoln, NE, and by the University of Nebraska Medical Center. Mr. Koundouno, Mr. Ifono, Mr. Millimono, Mr. Kourouma, Mr. Millimouno, and Mr. F. Tolno operate the Laboratoire des Fièvres Hémorragiques Virales de Guéckédou and are supported by the Ministère de la Santé et de l'Hygiène Publique in Guinea and the Direction Préfectorale de la Santé of Guéckédou.

Disclosure forms provided by the authors are available with the full text of this letter at NEJM.org.

1. Amman BR, Bird BH, Bakarr IA, et al. Isolation of Angolalike Marburg virus from Egyptian rousette bats from West Africa. Nat Commun 2020;11:510.

2. Brauburger K, Hume AJ, Mühlberger E, Olejnik J. Forty-five years of Marburg virus research. Viruses 2012;4:1878-927.

**3.** O'Hearn AE, Voorhees MA, Fetterer DP, et al. Serosurveillance of viral pathogens circulating in West Africa. Virol J 2016; 13:163.

 Baize S, Pannetier D, Oestereich L, et al. Emergence of Zaire Ebola virus disease in Guinea. N Engl J Med 2014;371:1418-25.
Keita AK, Koundouno FR, Faye M, et al. Resurgence of Ebola virus in 2021 in Guinea suggests a new paradigm for outbreaks. Nature 2021;597:539-43.

DOI: 10.1056/NEJMc2120183

# Association between Covid-19 Vaccination and Influenza Vaccination Rates

**TO THE EDITOR:** The polarizing nature of vaccination against coronavirus disease 2019 (Covid-19) within the United States threatens public health and has contributed to variable statewide vaccine uptake that ranged from 50 to 80% as of January 2022.<sup>1</sup> Given the divided national landscape and anecdotal evidence from our own patients, we hypothesized that low Covid-19 vaccination rates would be associated with decreases in influenza vaccination rates.

Using nationally representative data from the Centers for Disease Control and Prevention,<sup>2</sup> we calculated changes in influenza vaccine uptake at the state-population level during the pandemic after Covid-19 vaccines became widely available (September 2021 through January 2022) relative to before the pandemic (September 2019 through

January 2020). To account for pandemic-related factors unrelated to Covid-19 vaccines that might affect changes in influenza vaccine uptake (e.g., worsening inequities in access to care<sup>3,4</sup> or employment), we also compared September 2020 through January 2021 (the first influenza season during the pandemic but before widespread Covid-19 vaccine availability) to before the pandemic. We stratified changes in influenza vaccine uptake according to quartile of state-level cumulative Covid-19 vaccine uptake through January 2022. We used mixed-effects linear regressions (difference-in-differences analyses) to examine whether changes in influenza vaccine uptake during influenza seasons before as compared with during the pandemic differed between states with high as compared with low Covid-19

N ENGLJ MED 386;26 NEJM.ORG JUNE 30, 2022

The New England Journal of Medicine

Downloaded from nejm.org on July 10, 2022. For personal use only. No other uses without permission. Copyright © 2022 Massachusetts Medical Society. All rights reserved.