piravir and nirmatrelvir, respectively; and for the BA.5 subvariant, the IC_{50} was higher by factors of 1.2, 1.5, and 1.6 with remdesivir, molnupiravir, and nirmatrelvir, respectively (Table 1 and Fig. S4).

The main limitation of our study is the lack of clinical data on the efficacy of these monoclonal antibodies and antiviral drugs for the treatment of patients infected with BA.2.12.1, BA.4, or BA.5 subvariants. Overall, our data suggest that the three small-molecule antiviral drugs remdesivir, molnupiravir, and nirmatrelvir may have therapeutic value against the sublineages BA.2.12.1, BA.4, and BA.5 of SARS-CoV-2 omicron variants. Our data also indicate that bebtelovimab is effective against BA.2.12.1, BA.4, and BA.5. However, in clinical use, these variants may be less susceptible to combination therapy with casirivimab and imdevimab and with tixagevimab and cilgavimab. In addition, sotrovimab may not provide effective treatment against BA.2.12.1, BA.4, or BA.5. Our findings show that the selection of monoclonal antibodies to treat patients who are infected with omicron variants should be carefully considered.

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Supported by grants from the Center for Research on Influenza Pathogenesis (HHSN272201400008C, to Dr. Kawaoka) and from the Center for Research on Influenza Pathogenesis and Transmission (75N93021C00014, to Dr. Kawaoka), funded by the National Institutes of Allergy and Infectious Diseases; and by Research Program on Emerging and Reemerging Infectious Diseases (JP20fk0108412, to Dr. Kawaoka), Project Promoting Support for Drug Discovery (JP21nf0101632, to Dr. Kawaoka), the Japan Program for Infectious Diseases Research and Infrastructure (JP21wm0125002, to Dr. Kawaoka) from the Japan Agency for Medical Research and Development, and a grant-in-aid for Emerging and Reemerging Infectious Diseases from the Ministry of Health, Labor, and Welfare, Japan (20HA2007, to Dr. Hasegawa).

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

This letter was published on July 20, 2022, at NEJM.org.

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DOI: 10.1056/NEJMc2207519

A Zoonotic Henipavirus in Febrile Patients in China

TO THE EDITOR: The Hendra virus and the Nipah virus, which belong to the genus henipavirus in the family Paramyxoviridae, are known to infect humans and cause fatal disease; however, other related henipaviruses have been detected in bats, rodents, and shrews.[1-4] During sentinel surveillance of febrile patients with a recent history of animal exposure in eastern China, a phylogenetically distinct henipavirus, named Langya henipavirus (LayV), was identified in a throat swab sample from one patient by means of metagenomic analysis and subsequent virus isolation. The genome of LayV is composed of 18,402 nucleotides with a genome organization that is identical to that of other henipaviruses (Fig. 1A).[1] LayV is most phylogenetically related to Mojiang henipavirus, which was discovered in southern China (Fig. 1B).[3]

Subsequent investigation identified 35 patients with acute LayV infection in the Shandong and Henan provinces of China, among whom 26 were infected with LayV only (no other pathogens were present). These 26 patients presented with fever (100% of the patients), fatigue (54%), cough (50%), anorexia (50%), myalgia (46%), nausea (38%), headache (35%), and vomiting

(35%), accompanied by abnormalities of thrombocytopenia (35%), leukopenia (54%), and impaired liver (35%) and kidney (8%) function. A serosurvey of domestic animals detected seropositivity in goats (3 of 168 [2%]) and dogs (4 of 79 [5%]). Among 25 species of wild small animals surveyed, LayV RNA was predominantly detected in shrews (71 of 262 [27%]), a finding that suggests that the shrew may be a natural reservoir of LayV. (Additional details of the study are provided in the Supplementary Methods section in the Supplementary Appendix, available with the full text of this letter at NEJM.org.)

Although the current study does not fulfill Koch's postulates, the following findings from the patients with acute LayV infection suggest that LayV was the cause of febrile illness: LayV was the only potential pathogen detected in 26 of the 35 patients (74%) with acute LayV infection; in paired serum samples that were obtained from 14 patients during the acute and convalescent phases of infection, the IgG titers in 86% of the convalescent-phase samples were 4 times as high as those in the acute-phase samples; viremia was associated with acute LayV infection; and the patients with pneumonia had higher viral loads than those without pneumonia (mean [±SD] $\log_{10}$-transformed copies per milliliter, 7.64±0.98 vs. 4.52±1.13). Although human-to-human transmission has been reported for the Nipah virus,[5] we found no obvious spatial or temporal aggregation of human cases or the assigned haplotypes on the basis of three common single-nucleotide polymorphisms (Fig. 1C). There was no close contact or common exposure history among the patients, which suggests that the infection in the human population may be sporadic. Contact tracing of 9 patients with 15 close-contact family members revealed no close-contact LayV transmission, but our sample size was too small to determine the status of human-to-human transmission for LayV. The potential cross-reaction with Mojiang virus should be assessed to improve serologic testing.

In our study, a newly identified henipavirus of probable animal origin was associated with febrile illness, a finding that warrants further investigation to better understand associated human illness.

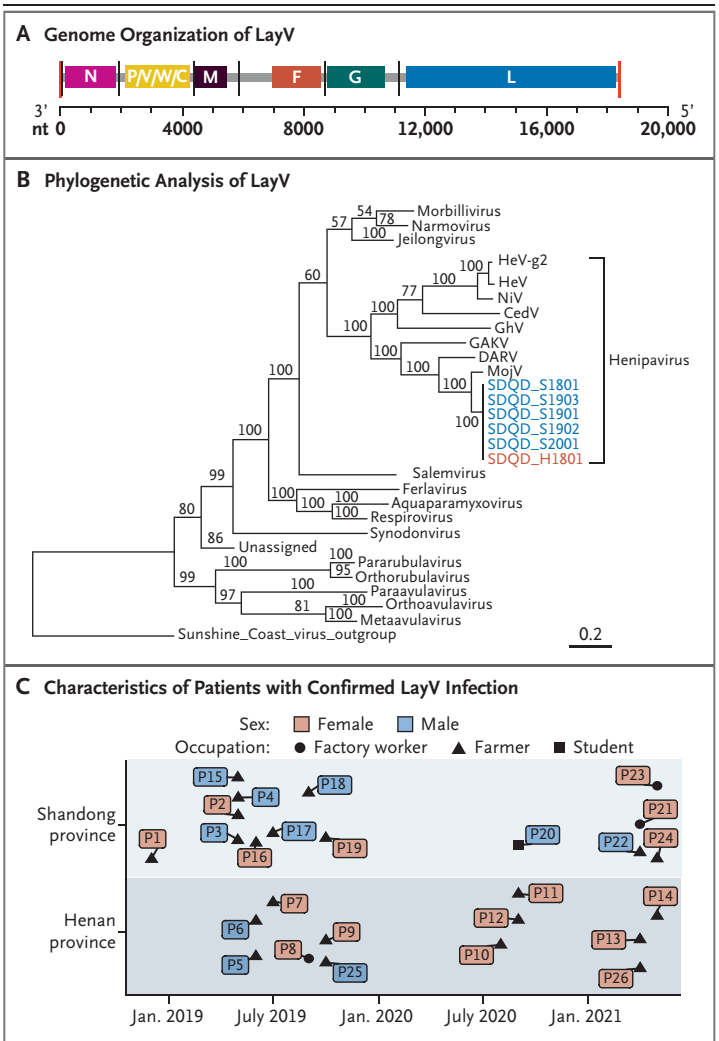

Figure 1. Genetic and Epidemiologic Characterization of LayV.

Panel A shows the genome organization of Langya henipavirus (LayV). The diagram is drawn to scale, and the scale bar is shown at the bottom. The abbreviation nt denotes nucleotides. Panel B shows the phylogenetic analysis of LayV. The tree was constructed on the basis of the complete amino acid sequence of RNA-directed RNA polymerase (the L protein) from LayV and other recognized species in the family Paramyxoviridae with the use of the maximum likelihood method. Recognized species in the family Paramyxoviridae were included in the analysis. LayV sequences obtained from humans and shrews are marked with red and blue, respectively. The scale bar denotes the number of nucleotide substitutions per site. Bootstrap testing (1000 replicates) was performed, and the bootstrap values are indicated. CedV denotes Cedar virus, DARV Daeryong virus, GAKV Gamak virus, GhV Ghana virus, HeV Hendra virus, HeV-g2 HeV genotype 2, MojV Mojiang virus, NiV Nipah virus, and SDQD Shandong Qingdao. Panel C shows the provincial location, occupation, sex, and temporal pattern of patients with confirmed LayV infection.

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Supported in part by a grant (81825019) from the National Natural Science Foundation of China. The work at Duke–National University of Singapore was supported by grants (NRF2012NRF-CRP001-056 and NRF2016NRF-NSFC002-013) from the National Research Foundation and by a grant (OFLCG19May-0034) from the National Medical Research Council, Singapore.

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

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DOI: 10.1056/NEJMc2202705

Childhood Risk Factors and Adult Cardiovascular Events

TO THE EDITOR: Jacobs et al. (May 19 issue)[1] explored the association of several childhood risk factors (body-mass index [BMI], systolic blood pressure, total cholesterol level, triglyceride level, and smoking status) with vascular events in adulthood. They found that there was an association between childhood risk factors and cardiovascular events in midlife. However, neither albuminuria nor the estimated glomerular filtration rate (eGFR) was assessed. Albuminuria and a decreased eGFR are key risk factors for cardiovascular events and, together with BMI, systolic blood pressure, lipid levels, and smoking, are used in adults to assess cardiovascular risk. An elevated eGFR may indicate actionable cardiovascular risk even when other risk factors indicate low risk.[2] Indeed, according to the 2021 European Society of Cardiology guidelines on cardiovascular disease prevention in clinical practice, the first step in risk stratification is the assessment of serum glucose and cholesterol levels, the eGFR, and the urinary albumin level.[2] In addition, albuminuria and the eGFR may be associated with several of the risk factors explored by Jacobs et al. Thus, the lack of assessment of albuminuria and the eGFR represents a limitation that was not mentioned in the article or in the accompanying editorial.[3]

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