viruses from 2022 had doubled ($\chi^2 = 55.3$; $p<0.0001$) (Appendix Figure). Those considerable changes in substitutions most likely reflect the editing activity of the human APOBEC3G enzyme (apolipoprotein B mRNA editing enzyme, catalytic subunit 3G), which catalyzes strand-specific C>U deamination, resulting in G>A substitutions in the complementary strand of viral genomes (A. O'Toole, unpub. data, https://virological.org/t/initial-observations-about-putative-apobec3-deaminase-editing-driving-short-term-evolution-of-mpxv-since-2017/830; [*9*]).

In conclusion, our analyses of MPXV genome sequences indicate that the virus has been circulating silently and undetected for about 2 decades, probably in multiple non–MPXV-endemic countries outside of Africa. Also, a clear genomic signature of a recent change in hosts is evidenced by major changes in its nucleotide substitution pattern. Our observations have major public health implications; the changing epidemiology of MPXV infections and human circulation of the virus in non–MPXV-endemic countries call for increased surveillance (*1*). The public health crisis caused by the COVID-19 pandemic may have favored the spread of MPXV under the radar in the past few years; however, the existence of asymptomatic carriers cannot be ruled out and may have contributed to the undetected spread of MPXV.

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References

1. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, et al. The changing epidemiology of human monkeypox—a potential threat? A systematic review. PLoS Negl Trop Dis. 2022;16:e0010141. https://doi.org/10.1371/journal.pntd.0010141
2. Antinori A, Mazzotta V, Vita S, Carletti F, Tacconi D, Lapini LE, et al.; INMI Monkeypox Group. Epidemiological, clinical and virological characteristics of four cases of monkeypox support transmission through sexual contact, Italy, May 2022. Euro Surveill. 2022;27:2200421. https://doi.org/10.2807/1560-7917.ES.2022.27.22.2200421
3. Isidro J, Borges V, Pinto M, Sobral D, Santos JD, Nunes A, et al. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. Nat Med. 2022;28:1569–72. https://doi.org/10.1038/s41591-022-01907-y
4. Saxena SK, Ansari S, Maurya VK, Kumar S, Jain A, Paweska JT, et al. Re-emerging human monkeypox: a major public-health debacle. J Med Virol. 2022;95:e27902. https://doi.org/10.1002/jmv.27902
5. Gigante CM, Korber B, Seabolt MH, Wilkins K, Davidson W, Rao AK, et al. Multiple lineages of monkeypox virus detected in the United States, 2021-2022. Science. 2022:378:560–5. https://doi.org/10.1126/science.add4153 PMID: 36264825
6. Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox virus in Nigeria: infection biology, epidemiology, and evolution. Viruses. 2020;12:1257. https://doi.org/10.3390/v12111257
7. Shackelton LA, Parrish CR, Holmes EC. Evolutionary basis of codon usage and nucleotide composition bias in vertebrate DNA viruses. J Mol Evol. 2006;62:551–63. https://doi.org/10.1007/s00239-005-0221-1
8. Bailey SF, Alonso Morales LA, Kassen R. Effects of synonymous mutations beyond codon bias: the evidence for adaptive synonymous substitutions from microbial evolution experiments. Genome Biol Evol. 2021;13:evab141. https://doi.org/10.1093/gbe/evab141
9. Yu Q, König R, Pillai S, Chiles K, Kearney M, Palmer S, et al. Single-strand specificity of APOBEC3G accounts for minus-strand deamination of the HIV genome. Nat Struct Mol Biol. 2004;11:435–42. https://doi.org/10.1038/nsmb758

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Epidemiology of SARS-CoV-2 Omicron BA.5 Infections, Macau, June–July 2022

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DOI: https://doi.org/10.3201/eid2902.221243

A SARS-CoV-2 Omicron BA.5 outbreak occurred in Macau from mid-June through July 2022. Out of >1,800 laboratory-confirmed cases, most were mild or asymptomatic; only 6 deaths were recorded. The outbreak was controlled through stringent public health and social measures, such as repeated universal testing and a stay-at-home order lasting 2 weeks.

The SARS-CoV-2 Omicron subvariant BA.5 has spread rapidly worldwide. A recent outbreak of BA.5 occurred in Macau during June 18–July 31, 2022. The outbreak resulted in 1,821 confirmed cases and 6 deaths but was promptly controlled. We describe the basic epidemiology of this outbreak.

Macau, a special administrative region of China with 683,000 persons, has been applying intensive public health and social measures to reduce SARS-CoV-2 variant importation and prevent community outbreaks as part of China's dynamic zero COVID strategy. In Macau, this strategy has included stringent travel restrictions and up to 28-day on-arrival quarantines (*1*) to avoid infections within communities. As in China, all SARS-CoV-2–infected persons are strictly isolated in special facilities, and contact tracing expedites timely quarantine of close contacts outside the home. Throughout the pandemic before June 2022, only 17 domestic confirmed cases (2.5 cases/100,000 population) and no deaths were reported in Macau. Since early 2021, inactivated virus (Sinopharm, http://www.sinopharm.com) and mRNA (Pfizer-BioNTech, https://www.pfizer.com) vaccines have been available in Macau. By June 19, 2022, vaccine coverage within the entire population was 85.6% for ≥2 doses and 40.5% for 3 doses.

In mid-June 2022, a SARS-CoV-2 Omicron BA.5 outbreak began in Macau (*2*). The first case was detected in a person with symptoms who sought treatment at a hospital on June 18, 2022. The source of infection remains unknown (*3*). Identification of a community outbreak prompted the government of Macau to impose a series of domestic public health and social measures to control local transmission (Appendix Table 1, https://wwwnc.cdc.gov/EID/article/29/2/22-1243-App1.pdf). Macau entered an immediate prevention state at 1:00 AM on June 19, 2022. Multiple rounds of universal PCR testing were

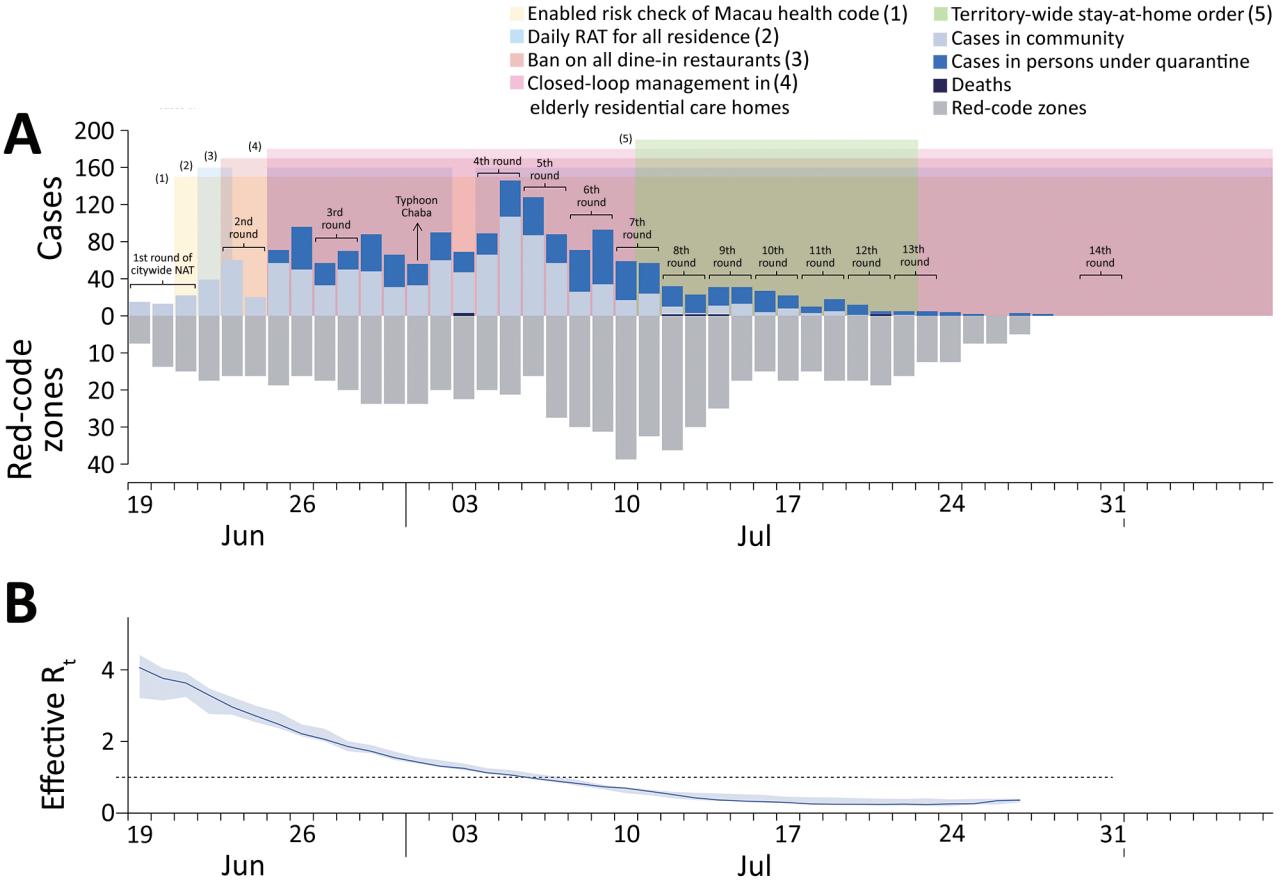

Figure. Number of PCR-positive COVID-19 cases and time-varying reproductive number in study of epidemiology of SARS-CoV-2 Omicron BA.5 infections, Macau, June–July 2022. A) PCR-confirmed COVID-19 cases and deaths in Macau during June and July 2022. Light blue bars indicate daily numbers of COVID-19 cases confirmed by PCR in the community; dark blue bars indicate persons under quarantine; black bars indicate number of reported deaths. Gray bars under the x-axis indicate the number of real-time red-code zones (areas with movement restrictions in place) in Macau. Shaded areas indicate when public health and social measures (indicated by numbers 1–5) were implemented to control COVID-19 transmission. B) Estimates of time-varying R_t to quantify real-time transmissibility of SARS-CoV-2 Omicron BA.5 in Macau. Dotted line indicates R_t of 1. RAT, rapid antigen test; R_t, effective reproductive number

Table. Estimated incubation periods for SARS-CoV-2 Omicron BA.5 variant according to population percentiles using lognormal, gamma, or Weibull probability distributions in study of epidemiology of SARS-CoV-2 Omicron BA.5 infections, Macau, June–July 2022*

Percentile	Incubation, d (95% CI)		
	Lognormal	Gamma	Weibull
Mean	3.27 (3.07–3.45)	3.00 (2.83–3.16)	3.26 (3.07–3.40)
2.5th	1.46 (1.17–1.74)	1.87 (1.74–2.00)	1.10 (0.93–1.25)
5th	1.64 (1.37–1.90)	2.02 (1.89–2.16)	1.38 (1.20–1.52)
50th	3.04 (2.87–3.18)	2.95 (2.79–3.12)	3.23 (3.03–3.38)
95th	5.67 (4.97–6.67)	4.13 (3.94–4.33)	5.24 (4.74–5.52)
97.5th	6.39 (5.49–7.77)	4.39 (4.19–4.59)	5.61 (5.05–5.94)
99th	7.34 (6.16–9.29)	4.70 (4.49–4.91)	6.03 (5.40–6.44)
AIC value†	360.80	377.57	370.45

*Mean number of days was estimated after adjusting for exponential growth. AIC, Akaike information criterion.
†AIC values were calculated to compare the fit of each model.

scheduled; and 14 rounds of citywide PCR testing were conducted for all persons in Macau. To identify infected persons, PCR testing was performed on June 22 and 25 for specific groups that included persons with Myanmar passports and those who sought care at places visited by persons who had SARS-CoV-2–positive tests (*4*,*5*). On June 23, schools, entertainment venues, public dining, and other nonessential businesses were closed, and residents were encouraged to stay at home. Closed-loop management was implemented in residential care homes beginning on June 25. Beginning on June 27, all persons were asked to conduct daily rapid antigen tests and report test results to an online platform (Appendix Tables 1, 2). The government enabled the risk check function of the Macau health code and implemented a district-specific epidemic prevention plan. Yellow- and red-code zones with movement restrictions were announced daily. As the daily case numbers grew, the government issued static management instructions comparable to a complete stay-at-home order beginning after midnight on July 11 and lasting until midnight on July 23; essential workers were excluded.

Among 1,821 cases that included 937 female and 884 male persons (3 months to 100 years of age), a total of 1,116 were classified as asymptomatic. The daily number of new positive cases peaked on July 5, 2022, at 146 PCR-positive cases (Figure 1, panel A). We estimated the time-varying reproductive number (Figure 1, panel B) to quantify real-time transmissibility (Appendix). The estimated time-varying reproductive number was <1 after July 7, 2022. In the final (14th) round of universal PCR testing on July 30–31, SARS-CoV-2 RNA was not found in specimens from persons in the community, confirming that the outbreak was contained.

Using information on 500 case-patients with known exposure and symptom onset reported during the early outbreak phase, we estimated that the mean incubation period for Omicron BA.5 was 3.27 days (SD ±1.05 days), after adjusting for exponential growth (*6*) (Table; Appendix Figure). The BA.5 incubation period was similar to 3.2 days for Omicron BA.1 (*7*) and 4.5 days for BA.2 (*8*) and shorter than that for other SARS-COV-2 variants (*9*).

Among 572 PCR-confirmed cases reported by June 30, a total of 23 case-patients had received 1 SARS-CoV-2 vaccine dose, 216 had received 2 vaccine doses, 224 had received 3 vaccine doses, and 109 were unvaccinated (Appendix Table 3). Although only 10% of the population was unvaccinated, 19% of the SARS-CoV-2–infected persons were unvaccinated.

Among the 1,821 locally infected case-patients, 6 deaths occurred (Appendix Table 4). Therefore, the case-fatality risk for Omicron-infected persons in Macau was 0.33% (95% CI 0.13%–0.76%). Persons who died of COVID-19 were 86–100 (mean 92.5, SD ±5.0) years of age. Among the 6 case-patients who died, 3 had received 2 doses of vaccine, and the other 3 were unvaccinated.

A limitation of our study is that we could not separate the effects of each public health and social measure because they were implemented as a package. High compliance with those stringent measures during the outbreak might have maximized the effectiveness of the interventions (*10*), although those measures might not be easily applicable to other locations outside of China. In conclusion, our study indicates that SARS-CoV-2 outbreaks can be controlled through stringent public health and social measures, such as repeated universal PCR testing and stay-at-home orders lasting at least 2 weeks.

Acknowledgments

We thank Julie Au for technical assistance.

This project was supported by the Collaborative Research Fund from the University Grants Committee of Hong Kong (project no. C7123-20G), Health and Medical Research Fund, Food and Health Bureau, Government of the Hong Kong Special Administrative Region, and Research Grants Council of Hong Kong Special Administrative Region, China (GRF 17110221).

B.J.C. reports honoraria from AstraZeneca, Fosun Pharma, GSK, Moderna, Pfizer, Roche, and Sanofi Pasteur. All other authors report no other potential conflicts of interest.

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References

1. Macao Government. Novel Coronavirus Response and Coordination Center of Macau. New epidemic prevention measures will be implemented from midnight on January 6. 2021 Dec 30 [cited 2022 Nov 14]. https://www.gcs.gov.mo/detail/zh-hans/N21LdGxjb9?8
2. Macau Government. Novel Coronavirus Response and Coordination Center of Macau. The virus in this outbreak is identified as Omicron BA.5. 2022 Jul 8 [cited 2022 Nov 14]. https://www.gcs.gov.mo/detail/zh-hans/N22GHgyjUl?4
3. Macau Government. Novel Coronavirus Response and Coordination Center of Macau. So far (20th) at 4 p.m., there have been 36 nucleic acid positive cases, and the two confirmed groups are related. 2022 Jun 20 [cited 2022 Nov 14]. https://www.gcs.gov.mo/detail/zh-hant/N22FTpK7To?30
4. Macau Government. Novel Coronavirus Response and Coordination Center of Macau. Novel Coronavirus Response and Coordination Centre announces nucleic acid testing arrangements in key areas and for key groups on June 22. 2022 June 22 [cited 2022 Nov 14]. https://www.gcs.gov.mo/detail/en/N22FU62sfT
5. Macau Government. Novel Coronavirus Response and Coordination Center of Macau. The Response and Coordination Centre announces the arrangements of the NAT for key areas tomorrow (25 June). 2022 June 25 [cited 2022 Nov 14]. https://www.gcs.gov.mo/detail/en/N22FYNcgqW
6. Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet Infect Dis. 2020;20:669–77. https://doi.org/10.1016/S1473-3099(20)30243-7
7. Backer JA, Eggink D, Andeweg SP, Veldhuijzen IK, van Maarseveen N, Vermaas K, et al. Shorter serial intervals in SARS-CoV-2 cases with Omicron BA.1 variant compared with Delta variant, the Netherlands, 13 to 26 December 2021. Euro Surveill. 2022;27:2200042. https://doi.org/10.2807/1560-7917.ES.2022.27.6.2200042
8. Mefsin YM, Chen D, Bond HS, Lin Y, Cheung JK, Wong JY, et al. Epidemiology of infections with SARS-CoV-2 Omicron BA.2 variant, Hong Kong, January–March 2022. Emerg Infect Dis. 2022;28:1856–8. https://doi.org/10.3201/eid2809.220613
9. Wu Y, Kang L, Guo Z, Liu J, Liu M, Liang W. Incubation period of COVID-19 caused by unique SARS-CoV-2 strains: a systematic review and meta-analysis. JAMA Netw Open. 2022;5:e2228008. PubMed https://doi.org/10.1001/jamanetworkopen.2022.28008
10. Zhou L, Wu Z, Li Z, Zhang Y, McGoogan JM, Li Q, et al. One hundred days of coronavirus disease 2019 prevention and control in China. Clin Infect Dis. 2021;72:332–9. https://doi.org/10.1093/cid/ciaa725

Serologic Evidence of *Orientia* Infection among Rural Population, Cauca Department, Colombia

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DOI: https://doi.org/10.3201/eid2902.221458

We assessed serum samples collected in Cauca Department, Colombia, from 486 persons for *Orientia* seroreactivity. Overall, 13.8% showed reactive IgG by indirect immunofluorescence antibody assay and ELISA. Of those samples, 30% (20/67) were confirmed to be positive by Western blot, showing ≥1 reactive band to *Orientia* 56-kD or 47-kD antigens.

Scrub typhus, caused by species in the genus *Orientia*, is a reemerging mite-borne rickettsiosis and a major cause of acute undifferentiated febrile illness (AUFI) (*1*). Classically, scrub typhus was believed to be strictly endemic to the so-called tsutsugamushi triangle, which ranges from southeastern Siberia in the North to the Kamchatka Peninsula in the East, northern Australia in the South, and Pakistan in the West (*1*). However, scrub typhus outside the tsutsugamushi triangle was suggested 70 years ago because