Use of Wastewater for Mpox Outbreak Surveillance in California

TO THE EDITOR: In May 2022, cases of mpox (formerly known as monkeypox) virus (MPXV) infection were reported outside regions in Africa where it is endemic. The global spread of MPXV infection, coupled with evidence of human-to-human transmission of a typically zoonotic disease, triggered a rapid scale-up of public health response, including surveillance to identify cases and guide local response.[1] However, access to and use of testing has been limited due in part to social stigma, difficulty recognizing a disease that is relatively new outside Africa, and potential for minimally symptomatic cases. A complementary surveillance approach that is independent of individual testing is through monitoring of wastewater, which represents a composite biologic sample from a community. The presence and concentration of pathogens that are shed into wastewater provide information about disease without the need for any involvement at the individual level, thereby offering an attractive means of attaining situational awareness for public health agencies and clinicians.

The use of wastewater surveillance for infectious diseases has grown rapidly with the enabling technology, and our team represents a collaboration between the California Department of Public Health and researchers who have been running a routine wastewater monitoring program since 2020. We have previously reported strong relationships between RNA from severe acute respiratory syndrome coronavirus 2,[2] respiratory syncytial virus,[3] and influenza A[4] found in wastewater and rates of associated diseases in the community. As part of the response to the spread of MPXV infection, we adapted and deployed polymerase-chain-reaction assays targeting MPXV genomic DNA[5] as part of our ongoing wastewater surveillance program. Testing was implemented within a month after the first identified case of MPXV infection in the United States, and the results were used in real time for the public health response in California.

MPXV DNA concentrations were measured daily in settled wastewater solid samples from nine wastewater plants between June 19 and August 1, 2022. During the study period, correlations between MPXV DNA concentrations and incident cases of MPXV infection that were reported from each sewershed (the geographic area including all the sewer lines that drain to a single access point) were estimated (Fig. 1). MPXV DNA was detected at all the study sites; five of nine sites detected MPXV DNA before or within a day after the first case had been identified in the corresponding sewershed. We observed a positive correlation between MPXV DNA in wastewater solids and the incidence of reported cases at the sites where positive samples were identified on more than 10 days. This strong relationship between MPXV DNA concentrations in wastewater and the incidence of MPXV infection suggests that wastewater surveillance is a viable method to monitor trends in MPXV activity. Additional details including validation with a second assay and comparisons between measurements from influent and settled solids are provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org.

Real-time results informed the state and local public health response, allowing for escalation of the state response level when detection in multiple watersheds suggested that MPXV was widespread or unexpected, alerting clinicians, and guiding the allocation of resources (e.g., testing, vaccines, and therapeutics) and personnel in affected areas. Our experience in adapting routine wastewater-surveillance infrastructure to monitor for a nonenteric, nonrespiratory virus such as MPXV shows promise for the future use of this method as an adjunct public health tool.

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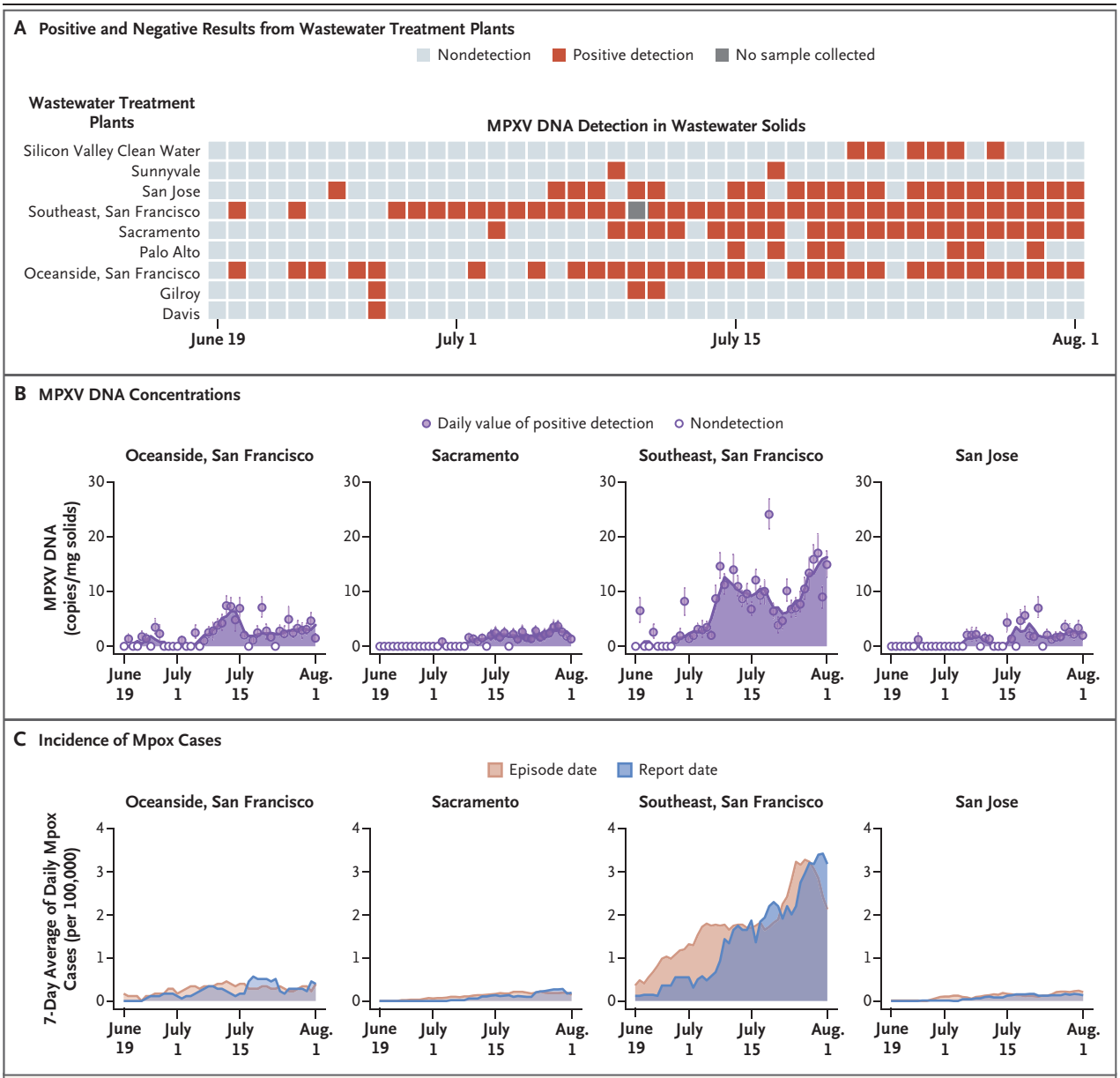

Figure 1. Mpox Virus (MPXV) in Wastewater and MPXV DNA Concentrations and Incidence of Mpox Cases According to Sewershed Location.

Panel A shows a heat map of positive and negative results from nine publicly owned wastewater treatment plants. Panel B shows a time series of concentrations of MPXV DNA in wastewater at the four selected publicly owned treatment plants with positive samples identified on more than 10 days during the study period. The area under the curve represents the 5-day trimmed average of MPXV DNA copies per milligram of wastewater solids. I bars indicate standard deviations and include the Poisson error and variability among the 10 replicates (68% confidence intervals reported by the instrument software as "total error"). Panel C shows the incidence of mpox cases, averaged over 7 days. Definitions of case variables are provided in the Supplementary Appendix.

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Early Active Mobilization during Mechanical Ventilation in the ICU

TO THE EDITOR: Previous investigations have shown that oversedation and immobilization of mechanically ventilated patients are associated with or result in greater length of hospital stay, decreased survival, and greater incidence of acquired dementia.[1-3] The evidence-based ABCDEF (analgesia monitoring and management, breaks daily from both sedation and ventilator use, choice of sedation [avoiding benzodiazepines], delirium monitoring and management, early mobility, and family engagement) safety bundle helps us rehumanize care and establish higher adherence to key steps; E (for early mobility) yields dose–response results of earlier discharge and greater survival.[4] The TEAM (Treatment of Mechanically Ventilated Adults with Early Activity and Mobilization) trial (Nov. 10 issue)[5] is a landmark achievement.

There was, however, a narrow separation between the intervention group and the control group, with only a 12-minute mean difference per day in mobilization owing to improvements in the control group as compared with earlier studies[3] and an unintended upper limit of mobility imposed by heavy sedation in patients in the intervention group (Figure S4 in the Supplementary Appendix of the article, available with the full text of the article at NEJM.org). Data regarding levels of consciousness may help explain upstream limitations on the intervention group that were caused by sedation practices. Figure S7 shows similarly high numbers of patients in both groups unable to make sustained eye contact (indicating a lack of separation between groups), as measured by a score of –2 or lower on the Richmond Agitation and Sedation Scale (RASS), which ranges from –5 (unresponsive) to 4 (combative); 97.8% of patients in the intervention group were receiving continuous sedative infusions at enrollment. Can the authors provide data regarding the ongoing frequency of sedative infusions and the daily mean doses of major sedatives according to trial group?

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