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SPECIAL ARTICLE

Monkeypox: Challenging Clinical Questions

In May 2022, monkeypox emerged in nonendemic regions of a world weary from years of dealing with COVID-19. The first U.S. case was reported on 17 May 2022, and on 4 August 2022 the Centers for Disease Control and Prevention (CDC) declared monkeypox a public health emergency. As of 30 September 2022, CDC was tracking 71 408 cases in more than 100 countries (1). Thankfully, as we approach mid-October 2022, the monkeypox outbreak seems to be ebbing. Among the 12 countries with the highest cumulative cases reported, the United States, Canada, and European countries are experiencing clear declines in incidence.

However, the virus remains a concern. As of 11 October 2022, there were 26 778 cases and 2 monkeypox-related deaths in the United States (1, 2). Monkeypox will likely continue to occur in previously nonendemic areas, although not at the dramatic rate initially feared. Consequently, clinicians need information about the prevention and management of an infection most have never encountered before. On 11 October 2022, *Annals of Internal Medicine* and the American College of Physicians gathered a panel of experts to provide that information in a virtual forum.

The panelists, all specialists in infectious diseases, were Dr. Roy M. Gulick (Rochelle Belfer Professor in Medicine, Weill Medical College of Cornell University), Dr. Cassandra M. Pierre (Assistant Professor of Medicine, Boston University Chobanian & Avedisian School of Medicine), and Dr. Stuart N. Isaacs (Associate Professor of Medicine, University of Pennsylvania Perelman School of Medicine). Dr. Deborah Cotton (Deputy Editor of *Annals of Internal Medicine* and Emerita Professor of Medicine, Boston University Chobanian & Avedisian School of Medicine) moderated the program. The program began with presentation of 3 clinical vignettes. After polling the participants about what they would do in each scenario, the panelists shared their own approaches. The panelists then addressed specific questions submitted by attendees.

The discussion covered a wide range of issues, such as the care of a patient at high risk for monkeypox infection but without a definite exposure; appropriate use of the only vaccine approved to prevent monkeypox; risk for transmission via various routes of exposure, including from contact with fomites; interventions to prevent spread in health care settings; and appropriate use of tecovirimat and other antiviral agents. The panelists largely agreed on the approaches to the clinical vignettes presented, but they repeatedly emphasized that we lack clinical trial evidence to define optimal use of vaccination and treatment.

While we continue to learn about modes of transmission, Dr. Pierre emphasized that it is largely via direct skin-to-skin contact or prolonged and close face-to-face contact. Although the virus can persist on surfaces and porous materials like bed linens, this does not to date seem to convey high risk. The CDC recommends that personal protective equipment in health care settings include masks, eye protection, gowns, and gloves. However, transmission in health care settings has not been observed during this outbreak, even among health care personnel with varied adherence to protective equipment (3).

Preventive strategies include avoiding high-risk behaviors and vaccinating individuals at risk for infection. The JYNNEOS vaccine is the only vaccine with U.S. Food and Drug Administration approval to prevent monkeypox infection. While the eligibility criteria for the vaccine were narrow early in the pandemic, the CDC has liberalized the criteria so that eligibility encompasses people who were exposed or are concerned they may have been exposed or may be exposed in the future. While single-dose regimens and intradermal dosing have been used or considered as strategies to stretch vaccine supply, the CDC recommends the approved 2-dose, subcutaneous regimen. A very important point made by the panelists is that persons previously vaccinated for smallpox should not assume that their prior vaccination protects them from monkeypox. If at risk for monkeypox, they should receive the JYNNEOS vaccine.

The panelists noted that tecovirimat was approved for the treatment of smallpox, not monkeypox, as part of bioterrorism preparedness and that approval was based on data in animals, not humans. Currently, tecovirimat is indicated for use in patients who are immunocompromised or who have severe disease characterized by widespread lesions, severe pain, and/or systemic symptoms. Tecovirimat's benefit is uncertain when prescribed for immunocompetent patients with milder illness. To provide needed evidence, Dr. Gulick encouraged clinicians to consider enrolling eligible patients in the STOMP trial (Study of Tecovirimat for Human Monkeypox Virus), a randomized trial of tecovirimat versus placebo in immunocompetent patients with mild disease (4). Administering tecovirimat to people with milder symptoms may increase the chance that the monkeypox virus develops resistance to the medication.

When contrasting recent experiences with COVID-19 and monkeypox, the panelists emphasized that we had a vaccine and an antiviral agent in our toolbox from the beginning of the monkeypox outbreak, whereas the COVID-19 toolbox was empty when COVID-19 emerged. However, making sure that the public health infrastructure

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is strong and stable is essential to effective and equitable use of available tools to save lives, reduce illness, and keep emerging diseases from becoming pandemics. Well-informed clinicians are also essential, so we encourage you to watch the video of this program.

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