



Viruses change; we can, too

Maybe we are coming out of the COVID-19 tunnel. Not that it is gone, it certainly is not. And we are currently dealing with the coincident impact of circulating influenza and respiratory syncytial viruses. But there was a sense of relative quiet on the infectious disease front. Then came monkeypox (mpox), a fairly unknown relative of the smallpox virus, with sinister implications. The questions of public health preparedness and social coping strategies came flooding back. Have we learned anything? Are we in a better position to deal with this than with COVID-19 or, for that matter, than we did initially with HIV? Fortunately, it seems that the answers are yes and yes, assisted by the limited lethality and public transmissibility of this infection—although as of February 1 this year, the US Centers for Disease Control and Prevention (CDC) website had reported 30,123 cases in the United States, with 28 deaths.

Mpox, a double-stranded DNA virus, was first identified in 1958 in a primate research colony in Denmark. It is an endemic animal infection in Central and Western Africa, affecting rodents, other small mammals, and nonhuman primates. The first human infection was reported in an African toddler in 1970. Sporadic human infections, primarily in Africa, were mainly attributed to direct contact with infected animals via bites, scratches, and the handling and preparation of infected meat. Cases outside that continent were associated with exportation of infected animals. Although there is shared immunity between smallpox and mpox viruses, the role that international smallpox vaccination has played in limiting mpox infection is unclear. Two major mpox variants (“clades”) have been described, each predominantly localized to a specific region in Africa, and each with overlapping but distinct clinical characteristics. Clade 1 exhibits a slightly higher morbidity and mortality than clade 2, possibly due to its ability to interfere with human complement activation. Double-stranded DNA viruses tend to have stable genomes and so do not mutate frequently.

In 2003, the CDC reported on 47 US cases of mpox. Patients were presumed to have contracted the virus from pet prairie dogs that had become infected from co-housed exotic mammals transported from Africa.¹ There was no confirmed person-to-person transmission. Human illness was assumed to have occurred through direct contact with infected animals, and perhaps via the upper respiratory tract. In one descriptive series of 34 patients (notably 50% female), 15% were severely ill, although none died, and 56% of the patients had the triad of rash, fever, and chills.² The rash was described as monomorphic in 68% and centrifugal in 48%, similar to that described previously in patients having contracted the infection from animals. By 2020, more than 80,000 human cases had been reported spanning 110 countries.

Forward to 2022, when significant local human clusters of mpox were reported in Europe and the United States,³⁻⁶ these outbreaks were characterized by direct human-to-human transmission. The initial source of these infections is not clear, but unique demographic and clinical characteristics of the infected persons are apparent. Reports stemmed from infectious disease and sexually transmitted disease clinics, and infected patients were overwhelmingly men who practice sex with men (MSM). There was a high proportion of skin lesions in genital and perianal areas as well as oral lesions and penile swelling. Adenopathy was common, as in earlier described patients, although seemingly more striking in the inguinal area. Pharyngitis and rectal pain were common. Of concern from the public health perspective is that some infected patients recalled no contact with persons having confirmed infections, and some infections were contracted from individuals who were asymptomatic at the time of sexual contact. Whether this is explained by the demon-

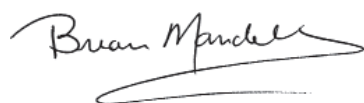
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strated presence of viral DNA in semen and other body fluids remains to be proven. Additionally, occupational spread to healthcare workers through sharp-instrument punctures has been described.

Has the mpox virus changed, or are we seeing the behavior of essentially the same virus manifesting in a specific host demographic by way of mucosal surface inoculation? The skin lesions may or may not spread from the genital, perianal, and oral areas, and may appear on the palms and soles and mimic other sexually transmitted infections including disseminated herpes and syphilis, particularly in immunosuppressed patients. Those with underlying HIV seem to fare less well. There continues to be an enormous male predominance, particularly including MSM, as noted in ongoing updates on www.cdc.gov.

So how has our reaction to this infection differed from prior international (and national) infection challenges? An early difference is that the World Health Organization in 2022—in an “aim to minimize unnecessary negative impact of names on trade, travel, tourism, or animal welfare, and avoid causing offence to any cultural, social, national, regional, professional, or ethnic groups”—proposed a name change to the virus (from monkeypox to mpox) and, for its previously geographically named major clades, a change to numbers and letters.⁷ Lesson learned from the apparent adverse social ramifications stemming from referring to coronavirus as “China flu.” There has also been a rapid recognition that although the current clusters are concentrated in the community of MSM, we have in the past clearly experienced specific demographic localized infections spreading to the wider population, and there needs to be wider vigilance for spread of the infection. This has been done without excessive stigmatization within the medical community.

Fortunately, there is already baseline knowledge about the mpox virus. As discussed by Sossai et al in this issue of the *Journal*,⁸ understanding its relationship to variola (smallpox) has been quickly exploited to provide some therapeutic and prophylactic vaccination options.



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