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Endemic Human Monkeypox, Democratic Republic of Congo, 2001–2004

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By analyzing vesicle fluids and crusted scabs from 136 persons with suspected monkeypox, we identified 51 cases of monkeypox by PCR, sequenced the hemagglutinin gene, and confirmed 94% of cases by virus culture. PCR demonstrated chickenpox in 61 patients. Coinfection with both viruses was found in 1 additional patient.

Monkeypox (MPX) virus is an orthopoxvirus that causes human MPX, a smallpox-like disease reported in the African rainforests. Humans acquire the virus through direct contact with infected animals or patients. To determine whether MPX virus could potentially occupy the niche vacated by smallpox virus, the World Health Organization (WHO) conducted an active surveillance program during 1981–1986 in the Democratic Republic of Congo (DRC) and identified 338 MPX cases (67% confirmed by virus culture). Epidemiologic data led to the conclusion that MPX was a sporadic disease with a low potential for person-to-person transmission and that infection could not sustain itself in the human population. In the following years (1986–1995), only 13 MPX cases were reported. However, during 1995–1996, >500 cases of suspected MPX were reported, although only a small number were laboratory confirmed. In contrast to the earlier findings by WHO, the percentage of secondary cases was much higher (78%) and the mortality rate was much lower (1.5%). The question was raised as to whether a number of these cases were actually chickenpox, caused by the varicella-zoster virus (VZV), which is characterized by a high rate of secondary transmission and a low mortality rate. Although MPX is the only known severe orthopoxvirus infection today, the current dynamics of MPX infection are poorly understood and little information is available to improve WHO recommendations for the prevention of human MPX. We report laboratory data obtained from patients with suspected MPX infection.

The Study
As part of the DRC Ministry of Health national disease surveillance program, 2,734 cases of suspected human MPX were reported from all 11 DRC provinces during January 2001–December 2004: 380 cases in 2001, 545 in 2002, 783 in 2003, and 1,026 in 2004. However, because civil war severely hampered surveillance activities, only 171 clinical specimens were obtained from 136 patients, who represent 4.9% of all reported cases. Ethical approval for this study was obtained from the Kinshasa School of Public Health, DRC, and the University of North Carolina, Chapel Hill, NC, USA.

All 171 specimens (crusted scabs and vesicle fluids) were inoculated onto MA104-cells by using standard procedures in a Biosafety Level 3 laboratory. Results yielded 56 MPX virus isolates from 48 patients (Table 1); scab and fluid specimens from the same patient were virus-positive for 8 patients. Identity of all isolates as MPX virus was confirmed by sequencing the entire open reading frame of the hemagglutinin (HA) gene.

DNA of all specimens was analyzed by using the RealArt Orthopox LightCycler PCR kit (QIAGEN, Hilden, Germany), which amplifies sequences of the fusion protein gene present in all orthopoxviruses, including MPX virus. Subsequent melting-curve analysis enables further differentiation of either variola or nonvariola orthopoxviruses; however, specific identification of MPX virus is not possible. We amplified nonvariola orthopoxvirus sequences in 65 specimens from 52 patients (Table 1); all specimens from which MPX virus had been isolated were also positive by PCR. For all 13 patients from whom crusts and vesicle fluids were available, both specimens were PCR-positive.

Of 171 specimens examined by using RealArt VZV LC PCR (QIAGEN), 78 showed specific amplification that indicated that 62 patients had VZV infection (Table 1). Of 136 patients investigated, 1 was coinfected with both, MPX (PCR and virus isolation) and VZV (PCR). Coinfections were reported during the 1996–1997 outbreak and in a patient who died in 2001. Whether these coinfections resulted from simultaneous circulation of both viruses or...
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Table 2. Age and sex distribution of patients with monkeypox or chickenpox, Democratic Republic of Congo, 2001–2004*

| Age, y | No. of patients investigated | MPX-positive | VZV-positive |
|-------|-----------------------------|--------------|--------------|
|       | male/female, n = 134        | male/female, n = 51 | male/female, n = 61 |
| ≤4    | 12/21                       | 8/7           | 3/6           |
| 5–14  | 22/19                       | 12/9          | 7/8           |
| 15–24 | 17/13                       | 5/7†          | 10/5†         |
| 25–34 | 9/8                         | 2/0           | 5/6           |
| ≥35   | 6/7                         | 1/0           | 5/6           |
| Total | 66/68                       | 28/23         | 30/31         |

*MPX, monkeypox; VZV, varicella-zoster virus.
†Coinfection with MPX and VZV in a 17-year-old female patient.
infection in humans because it causes disease clinically indistinguishable from smallpox. Recent outbreaks of MPX in the United States (13), the Republic of Congo (14) and Sudan (15) highlight the capacity of this virus to appear where it has never before been reported. Because clinically, MPX is often confused with chickenpox, laboratory diagnosis is critical to determine whether a suspected case is indeed MPX. In our study, we identified the causative agent for a rash-causing illness in 83% of all patients. We have recently strengthened the MPX surveillance program to improve understanding of the epidemiology of human MPX.

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