Monkeypox: what do we know about treatment and vaccination?

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Monkeypox is a viral infection, caused by the DNA virus monkeypox, part of the orthopox genus, in the family poxviridae. Although it is named "monkeypox" after first being identified in research monkeys, the original host is not known but is likely to be smaller rodents. Human monkeypox was first noted in the Democratic Republic of Congo in 1970. Typical symptoms include vesicles or ulceration and may include systemic symptoms such as fever, lymphadenopathy and myalgia. Monkeypox virus (MPXV) is spread by close contact with lesions of those infected and is spread via face-to-face, skin-to-skin, mouth-to-mouth or mouth-to-skin contact. The incubation period is typically 5-21 days. Monkeypox has previously been confined to Western and Central Africa, whereby two distinct clades have been identified, Clade I (formerly Congo Basin) and Clade II (West African). Imported cases of monkeypox have been reported sporadically in various countries, but sustained community transmission in countries that are not usually endemic have not been reported prior to May 2022.

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In May 2022, an increasing number of countries in Europe and the Americas reported cases of Monkeypox. Between 1 January 2022 and October 21 2022 a total of 75,441 laboratory confirmed cases have been reported to WHO[1]. The virus has mostly been identified amongst men who identify as Gay, Bisexual and Men who have Sex with Men (GBMSM), but this not always the case. Monkeypox, in the context of this outbreak, is described as mild with most people recovering without treatment, although in those who are immunocompromised monkeypox virus can be more severe[2]. Diagnosis is made by Polymerase Chain Reaction (PCR), which can be done on lesion swabs, throat swabs, or blood. Treatment options are not yet well established and options will be discussed.

In terms of prevention, Modified Vaccinia Ankara (MVA) can be used to prevent more serious complications. MVA is live attenuated vaccine, which contains modified vaccinia Ankara, a vaccinia virus closely related to smallpox[4]. Vaccinia Ankara does not cause disease in humans as it is unable to replicate. Similar antibodies are produced which are protective against MPXV. MVA is given intra-muscularly and most efficacious in the first four days following exposure, although some efficacy has been demonstrated up to 14 days following administration[4]. In a 2013 randomised control trial of over 4,000 participants, found no significant safety concerns and described a good tolerability profile[5]. Previous replication competent smallpox vaccines, such as DryVax, were associated with cardiac complications such as myocarditis and pericarditis[6], but this is not the case with MVA as adverse events in relation to the cardiovascular system were similar between the vaccinated group and placebo group[5]. Efficacy data for MVA against MPXV in humans is currently scarce. It is known that the virus is efficacious against smallpox and this knowledge is used to infer efficacy against monkeypox virus, alongside primate studies[7].

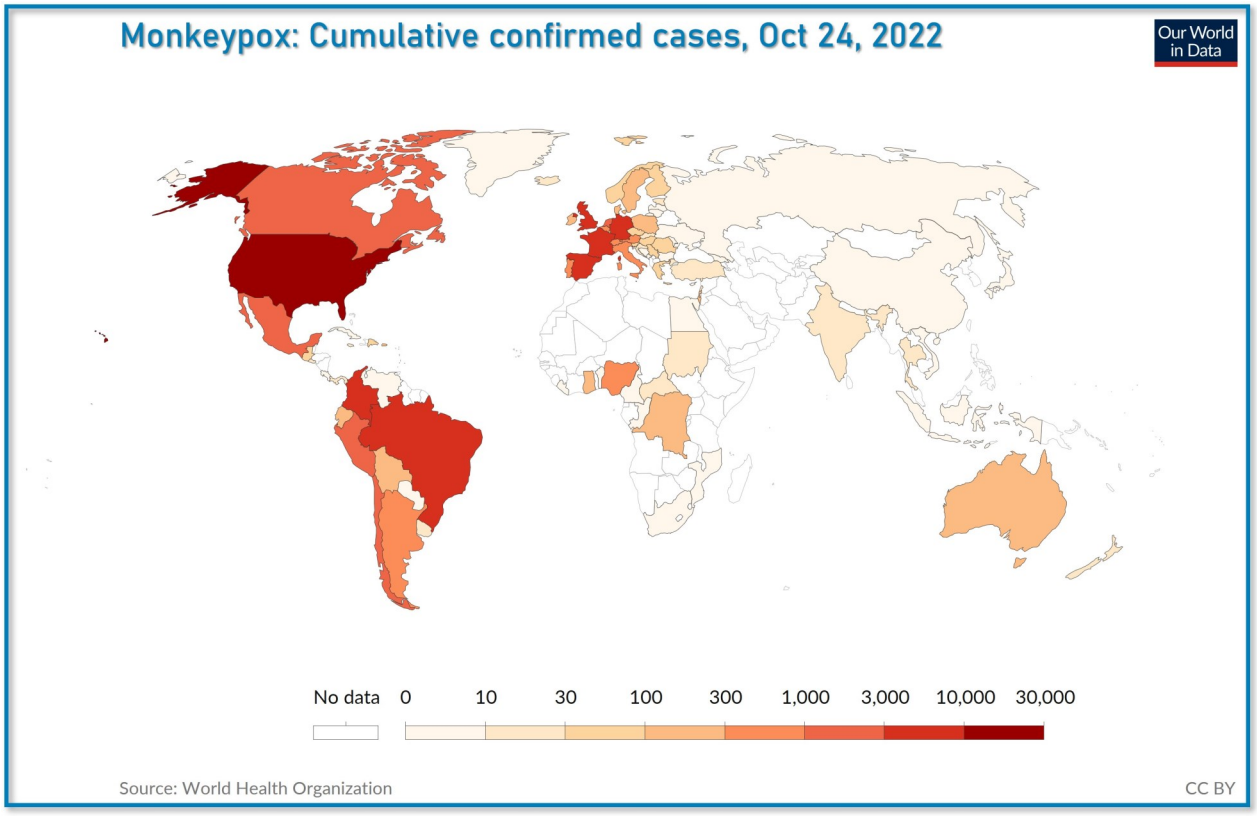
MVA is recommended for healthcare workers who may come in to contact with MPXV, laboratory workers who are likely to handle MPXV and those who have had close contact exposure to a case of confirmed MPXV. In the UK, the Joint Committee on Vaccination and Immunisation (JCVI) has also now recommended that GBMSM who are at highest risk are vaccinated with MVA[8].

At the start of the 2022 outbreak, there was no licensed treatment for MPXV in the UK. Treatment is based on knowledge of smallpox.

Tecovirimat has been used in the UK for inpatients with the severe disease. Tecovirimat, an anti-viral which inhibits p37, a protein present in orthopox viruses, has been used in the treatment of smallpox in animals and has a reasonable safety profile in humans[9]. In animal studies, Tecovirimat showed good efficacy, and the best outcome was when given in combination with post exposure prophylaxis MVA[10].

Cidofivir, an acyclic nucleoside analogue, is used for DNA virus infections, primarily CMV retinitis. It has known to have *in vitro* activity against orthopox viruses and *in vivo* activity against pox viruses in animal studies[13]. Cidofivir is used in humans, but there is caution over its safety profile given nephrotoxicity concerns[11].

Brincidofivir is a lipid analogue of Cidofivir. There is no human data available but it has been shown to be efficacious against MPXV *in vitro*[12]. In case reports, Brincidofivir has been shown to cause liver derangement and did not lead to any clinical benefit[13].



Vaccinia Immune Globulin Intravenous (VIGIV) may be a treatment option, but efficacy is not known[14] and access may be limited.

In summary, the 2022 monkeypox outbreak has risen rapidly and unexpectedly. It was reported in early 2022 that monkeypox may become a threat given the cessation of the smallpox vaccination[15], but it could not be predicted or expected that an outbreak of this scale would arise. With vaccinations being rolled out on a large scale, cohort data will become available in due course on MPXV protectivity of MVA. Similarly, observational data and planned clinical trials will provide further insight to MPXV treatment options.

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